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=> D HIS

     (FILE 'HOME' ENTERED AT 12:47:38 ON 26 JAN 2002)

     FILE 'HCAPLUS' ENTERED AT 12:47:48 ON 26 JAN 2002
L1          4356 S BROWN M?/AU
L2             6 S FEDECHKO P?/AU
L3          1566 S WONG J?/AU
L4          5934 S L1-3
L5             1 S L4 AND ?TETRALONE
L6             1 S L4 AND (HANSENULA OR H)(W)POLYMORPHA
L7             2 S L5-6
               SELECT HIT L7 1-2

     FILE 'REGISTRY' ENTERED AT 12:50:20 ON 26 JAN 2002
L8             6 S E1-6

     FILE 'HCAPLUS' ENTERED AT 12:50:41 ON 26 JAN 2002
L9             2 S L7 AND L8
L10          806 S (HANSENULA OR H)(W)POLYMORPHA
L11           10 S L10 AND (26012 OR 74449)
L12            2 S L10 AND (ATCC(W)26012 OR ATCC(W)74449)
L13           10 S L11 OR L12
L14           10 S L13 NOT L9
L15           22 S L10(L)REDUCTASE
L16            0 S L14 AND L15
L18           81 S L10 (L)PREP?
L19            1 S L18 AND PRECIPITAT?
L20            0 S L18 AND ?SUSPEND?
L21            1 S L18 AND ?SATURAT?
L22            1 S L18 AND ?GRADIENT?
L23            1 S L18 AND ?FRACTION?
L24            2 S L18 AND ??COLUMN?
L25            1 S L18 AND ??DESALT?
L26            0 S L18 AND ?PLOT?
L27            6 S L19 OR L21-25

     FILE 'REGISTRY' ENTERED AT 13:10:17 ON 26 JAN 2002
L28            4 S L8 AND C6-C6/ES

     FILE 'HCAPLUS' ENTERED AT 13:13:20 ON 26 JAN 2002
L29           48 S L28
L30           41 S L29 NOT (L9 OR L14 OR L15 OR L27)
L31            6 S L30 AND STEREOSELECT?
L32           35 S L30 NOT L31
               S 79560-19-3/RRG#

     FILE 'REGISTRY' ENTERED AT 13:20:55 ON 26 JAN 2002
L33            1 S 79560-19-3/RN

     FILE 'HCAPLUS' ENTERED AT 13:20:56 ON 26 JAN 2002
               S 9035-49-3/RRG#

     FILE 'REGISTRY' ENTERED AT 13:23:18 ON 26 JAN 2002
L34            1 S 9035-49-3/RN

     FILE 'HCAPLUS' ENTERED AT 13:23:19 ON 26 JAN 2002
L35          397 S L34
L36            2 S L9 AND (ATCC(W)26012 OR ATCC(W)74449 OR   (HANSENULA OR H)(W
L37            1 S L36 NOT L7
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inventor SEARCH

2 citations w/ 6 compounds displayed

10 cites related to claimed burg

22 cites related to reductases from H. polym.

purification terms

6 cites for prep of claimed burg

← 4 stereoisomers & a cpd where stereo-chem is not indicated in claim 2

6 cites for cpds

35 remaining cites for L28 cpds

← CAS # for any reductase w/unknown sequence

1 cite for reductase from H. polymorpha

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L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:[illegible] HCAPLUS
DOCUMENT NUMBER: 1[illegible]
TITLE: Stereoselective microbial or enzymic reduction of 3,5-dioxo esters to 5-hydroxy-3-oxo, 3-oxo-5-hydroxy, and 3,5-dihydroxy esters
INVENTOR(S): Patel, Ramesh N.; Banerjee, Clyde G.; Banerjee, Amit; Sharma, Vasanti J.
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 1[illegible] pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP [illegible]	A2	19931118	EP 1993-[illegible]	19930514
EP [illegible]	A3	1[illegible]		
EP [illegible]	B1	20001[illegible]		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US [illegible]	A	1[illegible]	US 1993-[illegible]	19930515
CA [illegible]	AA	19931116	CA 1993-[illegible]	19930416
JP [illegible]	A2	1994[illegible]	JP 1993-[illegible]	19930514
AT [illegible]	E	20001[illegible]	AT 1993-[illegible]	19930514
ES [illegible]	T3	2001[illegible]	ES 1993-[illegible]	19930514

PRIORITY APPLN. INFO.: US 1992-[illegible] A 19920515
OTHER SOURCE(S): MARPAT 120:[illegible]
AB Microorganisms or reductases derived from them reduce a dibenzyl ester, PhCH2OCH2CCOCH2COCH2CO2R2, R1=alkyl, cycloalkyl, aryl, aralkyl, cycloalkylalkyl; R2=alkyl) to form the assocd. 5-hydroxy, 3-hydroxy, or 3,5-dihydroxy esters. Selected microorganisms produce the preferred stereoisomers for use in the prepn. of antihypercholesterolemics. The Et ester of 3,5-dioxo-6-(benzyloxy)hexanoic acid was used as a test substrate in the screening of microorganisms for their ability to reduce it to the dihydroxy ester in phosphate buffer contg. glucose 750 mg/10 mL and substrate 25 mg/10 mL and a no. of suitable microorganisms identified. Conversion of the starting compd. was 15-85% with up to 97% of the conversion being the desired product. Further characterization of the reductase system in whole cells and cell exts. with purifn. of the reductase from exts. of Acinetobacter calcoaceticus ATCC 33305 is described.
IT **9037-80-3P**, Reductase
RL: IMF (Industrial manufacture); PREP (Preparation)
(purifn. of, from Acinetobacter calcoaceticus)
RN 9037-80-3 HCAPLUS
CN Reductase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> D IND

L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C12P007-62
ICS C07C067-31; C07C069-34; C12P041-06
IPA C12P007-62; C07C069-716; C07C069-708
ICI C12P007-62, C12R001-01, C12R001-645

CC 16-2 (Fermentation and Bioindustrial Chemistry)
ST dioxo ester microbial redn hydroxyester
IT Esters, reactions
RL: PREP (Preparation)
dioxo, prepn. and reactions of, in prepn. antihypercholesteremics, microbial redn. of dioxoesters in relation to)
IT Achromobacter
Acinetobacter
Acinetobacter calcoaceticus
Actinomyces
Alcaligenes
Arthrobacter
Arthrobacter simplex
Aspergillus
Azotobacter
Bacillus
Brevibacterium
Candida
Candida albicans
Corynebacterium
Curvulariamelia
Flavobacterium
Fusarium
Geotrichum
Geotrichum candidum
Hansenula
Hansenula polymorpha
Klebsiella
Mannyliomonas
Moniliella
Mycobacterium
Mycobacterium vaccae
Nocardia
Nocardia autotrophica
Nocardia globerula
Nocardia mediterranei
Nocardia restrictus
Nocardia salmonicolor
Penicillium
Pichia
Pichia methanolica
Pichia pastoris
Pseudomonas
Rhizopus
Rhodococcus
Rhodococcus equi
Rhodococcus fascians
Rhodococcus rhodochrous
Rhodopseudomonas
Rhodotorula
Saccharomyces
Saccharomyces cerevisiae
Streptomyces
Torulopsis
Trichoderma
Xanthomonas
(microbial redn. of dioxo esters with, in prepn. intermediates for synthesis of antihypercholesteremic)
IT Alcohols, reactions
Aldehydes, reactions

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reactions of, in prepn. antihypercholesteremics, microbial redn. of dioxoesters in relation to)

IT Ethers, reactions
RL: RCT (Reactant)
(1,2-di-, reactions of, in prepn. antihypercholesteremics, microbial redn. of dioxoesters in relation to)

IT Reduction
(biochem., stereoselective, of dioxoesters)

IT Esters, reactions
RL: RCT (Reactant)
(oxo, redn. of, microbial)

IT 152014-16-9P
RL: PREP (Preparation)
(prepn. of by microbial redn. of dioxo ester)

IT 92757-42-9P 152014-15-8P 152230-60-9P
RL: PREP (Preparation)
(prepn. of, by microbial redn. of dioxo ester)

IT **9037-80-3P**, Reductase
RL: PUR (Purification or recovery); PREP (Preparation)
(purifn. of, from Acinetobacter calcoaceticus)

IT 152014-14-7
RL: RCT (Reactant)
(redn. of, microbial)

L9 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:851764 HCAPLUS
DOCUMENT NUMBER: 136:2252
TITLE: Purification of reductase from **Hansenula polymorpha** useful for the stereoselective reduction of a racemic **tetralone**
INVENTOR(S): **Brown, Maria S.; Fedechko, Ronald W. ; Wong, John W.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
[illegible]	A1	20011122	US 2001-834098	20010412
			US 2000-200413 P	20000428

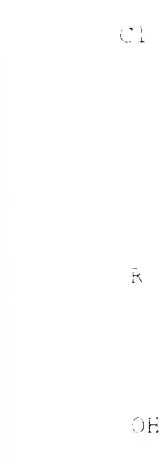
PRIORITY APPLN. INFO.:
GI

AB The present invention relates to novel compns. comprising an enzyme preparation capable of carrying out the following stereoselective redn. of a racemic **tetralone** I. Partial purifn. of a stereoselective reductase from **Hansenula polymorpha** is described. The resulting **tetralone** can be used in the synthesis of sertraline, which is known to be useful, for example, as an antidepressant and anorectic agent, and in the treatment of chem. dependencies, anxiety-related disorders, premature ejaculation, cancer and post-myocardial infarction.

IT **265126-78-1P 374777-87-4P**
RL: BSU (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(partial purifn. of reductase from **Hansenula polymorpha** useful for stereoselective redn. of racemic **tetralone**)

RN [illegible]-78-1 HCAPLUS
CN 1-Naphthalenol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-, (4R)- (9CI) (CA INDEX NAME)

Absolu[illegible]tereochemistry.



RN [illegible]-47-4 HCAPLUS
CN 1-Naphthalenol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-, (4S)- (9CI) (CA INDEX NAME)

Absolu[illegible]tereochemistry.

IT **124379-29-9P 155748-61-1P**
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(Purifn. of reductase from **Hansenula polymorpha** useful for stereoselective redn. of racemic **tetralone**)
RN 124[illegible]-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolu[illegible]tereochemistry. Rotation (+).

RN [illegible]-61-1 HCAPLUS
CN [illegible]-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 9037-80-3P, Reductase
RL: CAT (Catalyst use); PUR (Purification or recovery); PREP (Preparation); USES (Uses)
(purifn. of reductase from **Hansenula polymorpha** useful for stereoselective redn. of racemic **tetralone**)
RN [illegible]-80-3 HCAPLUS
CN [illegible] (9CI) (CA INDEX NAME)

*** STR [illegible] DIAGRAM IS NOT AVAILABLE ***
IT 79560-19-3
RL: [illegible] Reactant); RACT (Reactant or reagent)
(purifn. of reductase from **Hansenula polymorpha** useful for stereoselective redn. of racemic **tetralone**)
RN [illegible]-19-3 HCAPLUS
CN [illegible]-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

C1

=> d l [illegible] 2

L9 ANSWER [illegible] OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:290696 HCAPLUS
DOCUMENT NUMBER: 132:57351
TITLE: Stereoselective microbial reduction of a racemic **tetralone**
INVENTOR(S): Morse, Brock Knight; **Wong, John Wing**; Truesdell, Susan Jane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

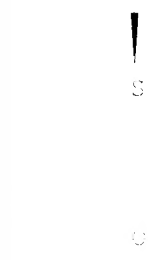
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP [illegible]	A2	20000503	EP 1999-308427	19991025
EP [illegible]	A3	20010103		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
AU [illegible]	A1	20000504	AU 1999-57787	19991018
JP 2000135098	A2	20000516	JP 1999-307272	19991028
JP 3106135	B2	20001106		
CN 1259651	A	20000607	CN 1999-123388	19991026
BR [illegible]	A	20001212	BR 1999-4964	19991026
JP [illegible]	A2	20010227	JP 2000-198150	19991028
PRIORITY APPLN. INFO.:			US 1998-106255 P	19981029
			JP 1999-307272 A3	19991028

GI

AB The present invention relates to novel processes for prepg. the (4S) enantiomer (I) of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (II) by stereoselective redn. of the racemic **tetralone** II to yield the (4R) tetralol (III), using a microorganism or an enzyme redn. system. I can be used in the synthesis of sertraline. The process further optionally comprises the sepn. of I from III. III can be recycled to give II and the process repeated to produce even more of the desired

IT **124379-29-9P**, 4S-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective microbial redn. of a racemic **tetralone**)
RN [illegible] HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



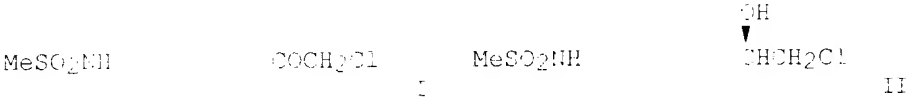
IT **79560-19-3**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: BPR (Biological process); RCT (Reactant); BIOL (Biological study); PROC (Process)
(stereoselective microbial redn. of a racemic **tetralone**)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

IT **265126-78-1P**
RL: BYP (Byproduct); PREP (Preparation)
(stereoselective microbial redn. of a racemic **tetralone**)
RN [illegible]-1 HCAPLUS
CN 1-Naphthalenol, 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

=> D IBIB ABS L14 1

L14 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:577774 HCAPLUS
DOCUMENT NUMBER: 121:177774
TITLE: Stereoselective microbial reduction of N-[4-(1-oxo-2-chloroacetyl ethyl) phenyl methane sulfonamide
AUTHOR(S): Patel, Ramesh N.; Banerjee, Amit; McNamee, Clyde G.; Szarka, Laszlo J.
CORPORATE SOURCE: Bristol-Myers Squibb Pharm. Res. Inst., New Brunswick, NJ, 08903, USA
SOURCE: Appl. Microbiol. Biotechnol. (1993), 40(2-3), 241-5
CODEN: AMBIDG; ISSN: 0175-7598
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II

AB Several microbial cultures were screened for the ability to catalyze the redn. of N-(4-(1-oxo-2-chloroacetyl ethyl)) Ph methane sulfonamide (I). The chiral intermediate (+)N-(4-(1-hydroxy-2-chloroethyl))phenyl methane sulfonamide (II) was prepd. by the stereoselective microbial redn. of the parent ketone I. Compd. II is a potential chiral intermediate for synthesis of 4-(2-isopropylamino-1-hydroxyethyl)phenyl methanesulfonanilide (D-sotalol), a beta-receptor antagonist. Microorganisms from the genera Rhodococcus, Nocardia, and Hansenula reduced I to II. A reaction yield of >50% and optical purities of >90% were obtained. The best strain (**H. polymorpha ATCC 26012**) effectively reduced compd. I to compd. II in 95% reaction yield and 99% optical purity. Compd. II (8.2 g) was isolated from a 3-l preparative batch in 68% overall yield. Isolated compd. II had a sp. rotation of +20.degree. (CH_2Cl_2, 3-l), an optical purity of 99.5%, and a chem. purity of 97% as analyzed by gas chromatog. and HPLC. The NMR and mass spectra of compd. II prepd. by bioredn. and a std. chem. sample of II were virtually identical. Cell exts. of **H. polymorpha** in the presence of glucose dehydrogenase, glucose and NAD catalyzed the redn. of I to II with 98% reaction yield and resulted in an optical purity of 99.4%.

=> D IBIB ABS L14 2

L14 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:535052 HCAPLUS
DOCUMENT NUMBER: 119:135252
TITLE: Microbial reduction of 1-(4-fluorophenyl)-4-[4-(5-fluoro-2-pyrimidinyl)-1-piperazinyl]butan-1-one
AUTHOR(S): Patel, Ramesh N.; Banerjee, Arnit; Liu, Mark; Hanson, Ronald; Ko, Raphael; Howell, Jeffrey; Szarka, Laszlo J.
CORPORATE SOURCE: Dep. Microb. Technol., Bristol-Myers Squibb Pharm. Res. Inst., New Brunswick, NJ, 08903, USA
SOURCE: Biotechnol. Appl. Biochem. (1993), 17(2), 139-53
CODEN: BABIEO; ISSN: 0885-4513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Among various microorganisms screened for the stereoselective redn. of 4-chloro-1-(4-fluorophenyl)butan-1-one (I), **Hansenula polymorpha** [American Type Culture Collection (A.T.C.C.) **26012** and 26014], Nocardia salmonicolor [Squibb Culture (S.C.) 6770], Arthrobacter simplex (A.T.C.C. 6949), Mycobacterium vaccae (A.T.C.C. 29678), Candida boidinii (A.T.C.C. 13801) and Saccharomyces cerevisiae (A.T.C.C. 13792) reduced I to the corresponding (R)-(+)-alc. (II). In contrast, Lactobacillus kefir (A.T.C.C. 35411), Pullularia pullulans (A.T.C.C. 16623), Trigonopsis variabilis (A.T.C.C. 10679) and Cunninghamella echinulata (A.T.C.C. 36569) reduced I to the (S)-(-)-alc. (IV). When 1-(4-fluorophenyl)-4-(1-piperazinyl)butan-1-one (III) was used as substrate for the redn., only Nocardia globerula (A.T.C.C. 12505) and Saccharomyces cerevisiae (A.T.C.C. 13792) converted compd. III into the corresponding (R)-(+)-alc. (V). Organisms which reduced compd. I were inactive for the redn. of compd. III. 1-(4-Fluorophenyl)-4-[4-(5-fluoro-2-pyrimidinyl)-1-piperazinyl]butan-1-one (5) was reduced to the corresponding (R)-(+)-alc. (VI) by Hortiereila ramanniana (A.T.C.C. 38191) and to the (S)-(-)-alc. (VII) by Pullularia pullulans (A.T.C.C. 16623). (R)-(+)-compd. V and compd. IV are key chiral intermediates in the total chem. synthesis of (R)-(+)-compd. VI, an effective antipsychotic agent under development at Bristol-Myers Squibb. A single-stage (fermn./biotransformation) process and two-stage (fermn. and subsequent biotransformation) process and two-stage (fermn. and subsequent biotransformation by cell suspensions) process were developed for the stereoselective redn. of compd. V to (R)-(+)-compd. VI. The enzyme which catalyzed the redn. of compd. V to (R)-(+)-compd. VI was purified to homogeneity. The purified protein consisted of a single polypeptide of 29 kDa.

=> D IBIB ABS L14 3

L14 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:4610 HCAPLUS
DOCUMENT NUMBER: 102:4610
TITLE: Enzymic hydrolysis of single cell protein
AUTHOR(S): Chen, Hui Fen; Yang, Ming Tung; Fang, Hong Yuan
CORPORATE SOURCE: Refin. Mfg. Res. Cent., Chin. Pet. Corp., Taiwan
SOURCE: Chung-kuo Nung Yeh Hua Hsueh Hui Chih (1984), 22(1-2), 119-27
CODEN: CKNHAA; ISSN: 0578-1736
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB **Hansenula polymorpha (ATCC 26012)**, a MeOH-grown yeast, was partially hydrolyzed by adding proteases and 5'-phosphodiesterase. The autolyzed yeast contg. small peptides and 5'-nucleotides can be used as seasoning ingredients in the food industry. Yeast cells were incubated with proteases under the following conditions: substrate concn., 10% (wt.%); enzyme-substrate ratio, 0.2% (0.1% crude papain and 0.1% bromelain, crude papain contg. 5'-phosphodiesterase). Yeast autolysis was carried out at 55.degree. and a pH of 5.5-6.0 for 4-24 h, and then heated up to 65.degree. for 60-70 min. The resulting autolyzed yeast was then directly freeze-dried. Sol. protein, in vitro digestibility, and taste testing of products were detd. for the autolysates of freeze-dried cells, spray-dried cells, spray-dried cells after Dyno mill treatment, and fresh cells, resp.: (1) percentage of sol. protein; 63-67, 61-68, 70-76, 76-78%, (2) in vitro digestibility; 75-78, 73-77, 75-80, 86-91%; (3) threshold concn. of taste: 2.5-2.8, 1.2-2.5, 1.0-1.2, 2.0-2.5%.

=> D IBIB ABS L14 4

L14 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:424447 HCAPLUS
DOCUMENT NUMBER: 93:24447
TITLE: Immobilized yeast cells with methanol oxidase activity: preparation and enzymic properties
AUTHOR(S): Couderc, R.; Baratti, J.
CORPORATE SOURCE: Cent. Biochim. Biol. Mol., CNRS, Marseille, 13274/2, Fr.
SOURCE: Biotechnol. Bioeng. (1980), 22(6), 1155-73
CODEN: BIBIAU; ISSN: 0006-3592
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cells of **Hansenula polymorpha** (**ATCC 26012**) were successfully immobilized by entrapment in a polyacrylamide gel. The resulting gel showed high methanol oxidase [9073-53-4] activity, esp. after treatment with a detergent. The enzymic properties of the gel-entrapped cells were not very different from that of the soln. enzyme except that no inhibition was obsd. at high MeOH [67-56-1] concn. In continuous reactors, the gel-entrapped cells showed a much higher stability than other enzyme prepns. The inactivation mechanism was investigated and proved to be the oxidn. of essential SH group(s) of the methanol oxidase mol. by H2O2. Treatment with .beta.-mercaptoethanol prevented inactivation or regenerated activity.

=> D IBIB ABS L14 5

L14 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:106284 HCAPLUS
DOCUMENT NUMBER: 92:106284
TITLE: Microbial production of methyl ketones. Purification and properties of a secondary alcohol dehydrogenase from yeast
AUTHOR(S): Patel, Ramesh N.; Hou, Ching T.; Laskin, Allen I.; Derelanko, Patricia; Felix, Andre
CORPORATE SOURCE: Corp. Pioneering Res. Lab., Exxon Res. Eng. Co., Linden, NJ, USA
SOURCE: Eur. J. Biochem. (1979), 101(2), 401-6
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell-free exts. derived from yeasts Candida utilis ATCC 26387, **Hansenula polymorpha ATCC 26012**, Pichia species NRRL-Y-11328, Torulopsis species strain A, and Kloeckera species strain A2 catalyzed an NAD-dependent oxidn. of secondary alcs. (2-propanol, 2-butanol, 2-pentanol, 2-hexanol) to the corresponding Me ketones (acetone, 2-butanone, 2-pentanone, 2-hexanone). A NAD-specific secondary alc. dehydrogenase from MeOH-grown yeast, Pichia species, was purified. The purified enzyme was homogeneous as judged by polyacrylamide gel electrophoresis. The purified enzyme catalyzed the oxidn. of secondary alcs. to the corresponding Me ketones in the presence of NAD as an electron acceptor; primary alcs. were not oxidized. The optimum pH for oxidn. of secondary alcs. was 8.0. The mol. wt. of the purified enzyme as detd. by gel filtration was 98,000 and the subunit size as detd. by Na dodecyl sulfate gel electrophoresis was 46,000. The activity of the purified secondary alc. dehydrogenase was inhibited by SH-group inhibitors and metal-binding agents.

=> D IBIB ABS L14 6

L14 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:571344 HCAPLUS
DOCUMENT NUMBER: 91:171344
TITLE: Oxidation of secondary alcohols to methyl ketones by yeasts
AUTHOR(S): Patel, R. N.; Hou, C. T.; Laskin, A. I.; Derelanko, P.; Felix, A.
CORPORATE SOURCE: Corp. Pioneering Res. Lab., Exxon Res. and Eng. Co., Linden, NJ, 07036, USA
SOURCE: Appl. Environ. Microbiol. (1979), 38(2), 219-23
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell suspensions of yeasts, Candida utilis ATCC 26387, **Hansenula polymorpha ATCC 26012**, Pichia NRRL-Y-11328, Torulopsis strain A1, and Kloeckera strain A2, grown on various C-1 compds. (MeOH, methylamine, methylformate, EtOH, and propylamine) catalyzed the oxidn. of secondary alcs. to the corresponding Me ketones. Thus, isopropanol, 2-butanol, 2-pentanol, and 2-hexanol were converted to acetone, 2-butanone, 2-pentanone, and 2-hexanone, resp. Cell-free exts. derived from MeOH-grown yeasts catalyzed an oxidized NAD-dependent oxidn. of secondary alcs. to the corresponding Me ketones. Primary alcs. were not oxidized. The effect of various environmental factors on the prodn. of Me ketones from secondary alcs. by MeOH-grown Pichia was investigated.

=> D [illegible] L14 7

L14 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:503300 HCAPLUS
DOCUMENT NUMBER: 89:103300
TITLE: The lipid component of two methanol-assimilating yeasts
AUTHOR(S): Mattray, James B. M.; Hambleton, James E.
CORPORATE SOURCE: Dep. Chem., Univ. Guelph, Guelph, Ont., Can.
SOURCE: Biochem. Soc. Trans. (1978), 6(2), 382-3
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the presence of 1% MeOH, Candida boidinii (ATCC 18810) had protein and lipid contents of 40.6 and 6.9%, resp., and **Hansenula polymorpha** (**ATCC 26012**) had contents of 32.4 and 5.2%, resp. Thin-layer chromatog. showed that the nonpolar component for both yeasts was composed of nonesterified fatty acid, triacylglycerol, and sterol. Phospholipid was the major lipid component, and for C. boidinii and **H. polymorpha** was composed of phosphatidylcholine, 46.6 and 39.8%, resp.; phosphatidylserine + phosphatidylinositol, 26.5 and 25.9%, resp.; phosphatidylethanolamine, 13.[illegible] and 4.5%, resp.; phosphatidylglycerol + diphosphatidylglycerol, 9.4 and [illegible]%, resp.; and others 15%. Both yeasts produced large amts. of unsatd. fatty acids.

=> D IBIB ABS L14 8

L14 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:599164 HCAPLUS
DOCUMENT NUMBER: 87:199164
TITLE: Yeast cells
INVENTOR(S): Kurimura, Yasuo; Takeuchi, Hideaki; Shimada, Masao
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Japan. Kokai, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP [illegible]4478	A2	19770809	JP 1976-8333	19760130

AB Cells of a Hansenula cultured on a MeOH [67-56-1]-medium were washed with water, lower alcs., or a mixt. of water and a lower alc. to yield yeast cells free of HCHO. Thus, cells of **Hansenula polymorpha ATCC 26012** continuously cultured on a MeOH-medium and contg. 6.5 ppm HCHO were washed with MeOH at room temp. for 1 h to yield cells without HCHO.

=> D [illegible] L14 9

L14 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:599163 HCAPLUS
DOCUMENT NUMBER: 87:199163
TITLE: Yeast cells
INVENTOR(S): Kurimura, Yasuo; Takeuchi, Hideaki; Shimada, Masao
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Japan. Kokai, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP [illegible]4477	A2	19770809	JP 1976-8332	19760130

AB Hansenula was cultured on a MeOH [67-56-1]-contg. medium until the MeOH concn. decreased to <0.1 wt.%, to yield yeast cells free of HCHO. Thus, **H. polymorpha ATCC 26012** was continuously cultured at 37.degree. and at various diln. rates on a liq. medium contg. 1% MeOH. HCHO was not detected in the cells when residual MeOH was <0.1%.

=> D [illegible] L14 10

L14 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:58[illegible] HCAPLUS
DOCUMENT NUMBER: [illegible]7:1826[illegible]
TITLE: Coenzyme Q7 production by yeast
INVENTOR(S): Kurimura, Yasuo; Miyauchi, Ominobu; Mori, Ichiko
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Japan. Kokai, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP [illegible]90692	A2	19770730	JP 1976-5407	19760122
JP [illegible]42276	B4	19811003		

AB Coenzyme Q7 [303-95-7] was produced by Hansenula by culturing on a MeOH [67-56-1] medium. Thus, H. polymorha **ATCC 26012** was aerobically cultured at 30.degree. for 60 h on a medium (pH 6.0) contg. MeOH 20, yeast ext. 2, and corn steep liquor 2 g to yield 50 g intact cells. The cells were suspended in 10 mL water then MeOH 100 mL, pyrogallol 5 g, and 60% NaOH 5 mL were added, the mixt. was heated at 85.degree. for 1 h with refluxing, 400 mL water was added, and the mixt. was cooled and extd. with 200 mL hexane. The ext. was wasned with water, dried with Na2SO4, the hexane evapd., and the residue was dissolved in 10 mL acetone and evapd. to dryness. Coenzyme Q7 was purified by alumina chromatog. to yield 25 mg yellow crude crystals.

=> D [illegible] L15 1-22

L15 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:913687 HCAPLUS
TITLE: Nitrogen metabolite repression in Hansenula polymorpha: the nmr1-1 mutation
AUTHOR(S): Serrani, Federica; Rossi, Beatrice; Berardi, Enrico
CORPORATE SOURCE: Dipartimento di Biotecnologie Agrarie ed Ambientali, Laboratorio di Genetica Microbica, Universita degli Studi di Ancona, Via Brecce Bianche, Ancona, 60131, Italy
SOURCE: Current Genetics (2001), 40(4), 243-250
CODEN: CUGED5; ISSN: 0172-8083
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In **Hansenula polymorpha**, the expression of the nitrate assimilation metab. is subjected to repression-derepression mechanisms triggered by reduced nitrogen cmpds. such as ammonium. To further our knowledge on the genetics of these regulatory mechanisms, a screening strategy for the isolation of mutants exhibiting nitrate **reductase** activities in the presence of reduced nitrogen cmpds. was set up. This strategy makes use of a nitrate- methylamine- mutant to isolate suppressors of its characteristic phenotype - the inability to grow on a nitrate plus methylamine medium. A total of 31 regulatory mutants were isolated with this strategy and grouped into five complementation classes. One of these mutants harbours the recessive mutation nmr1-1, which dets. the derepression of the nitrate assimilation metab. in media contg. nitrate plus a repressing nitrogen source (ammonium, methylamine, glutamate, urea or aspartate). Therefore, nitrate **reductase** activities are detected in the presence of reduced nitrogen sources, as long as nitrate is also in the medium. Our data indicate that the pathways of repression-derepression and induction are controlled by elements which are distinct. Furthermore, they indicate that Nmr1p is involved in repressing circuits which control not only the nitrate-utilization pathway, but also other pathways which are necessary for the utilization of nitrogen sources alternative to ammonium. Of considerable interest is the fact that our nmr1-1 mutant is derepressed in glutamate but not in glutamine. Since the phenotype of this mutant seems to include a glutamine synthetase defect, we suggest that glutamate (or a deriv. of this compd.) might be involved in signalling nitrogen metabolite repression in **H. polymorpha**. Thus, in **H. polymorpha**, a glutamine-dependent circuit may co-exist with a glutamine-independent circuit.

L15 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:851764 HCAPLUS
DOCUMENT NUMBER: 136:2252
TITLE: Purification of **reductase** from **Hansenula polymorpha** useful for the stereoselective reduction of a racemic tetralone
INVENTOR(S): Brown, Maria S.; Fedechko, Ronald W.; Wong, John W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 1744142	A1	20011122	US 2001-834098	20010412
			US 2000-200413 P	20000428

PRIORITY APPLN. INFO.:
GI

AB The present invention relates to novel compns. comprising an enzyme [illegible] capable of carrying out the following stereoselective redn. of a [illegible] tetralone I. Partial purifn. of a stereoselective **reductase** from **Hansenula polymorpha** is described. The chiral tetralone can be used in the synthesis of sertraline, well known to be useful, for example, as an antidepressant and anorectic agent, and in the treatment of chem. dependencies, anxiety-related disorders, premature ejaculation, cancer and post-myocardial infarction.

L15 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2004 ACS
ACCESSION NUMBER: 2001:44013 HCAPLUS
DOCUMENT NUMBER: 134:249364
TITLE: Evidence for multiple nitrate uptake systems in the yeast Hansenula polymorpha
AUTHOR(S): Machin, F.; Perdomo, G.; Perez, M. D.; Brito, N.; Siverio, J. M.
CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Grupo del Metabolismo del Nitrogeno-Consejo Superior de Investigaciones Cientificas, Universidad de La Laguna, La Laguna, Tenerife, E-38206, Spain
SOURCE: FEMS Microbiol. Lett. (2001), 194(2), 171-174
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Hansenula polymorpha** mutants disrupted in the high-affinity nitrate transporter gene (YNT1) are still able to grow in nitrate. To detect the nitrate transporter(s) responsible for this growth in a strain contg. disruption of the nitrate assimilation gene cluster and the gene encoding nitrate **reductase** gene (YNR1) under the control of the **H. polymorpha** MOX1 (methanol oxidase) promoter was used (YNT1- strain). In this strain nitrate taken up is transformed into nitrite by nitrate **reductase** and excreted to the medium where it is readily detected. Nitrate uptake which is neither induced by nitrate

[illegible] repressed by reduced nitrogen sources was detected in the FM31 strain. [illegible], nitrate uptake detected in the strain FM31 is independent of both Ynt1p and Ynt4p and is not affected by ammonium, glutamine or [illegible]. The inhibition of nitrate extrusion by extracellular nitrite suggests that the nitrate uptake system shown in the FM31 strain could also be involved in nitrate uptake.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:41195 HCAPLUS
DOCUMENT NUMBER: 132:21768
TITLE: A set of Hansenula polymorpha integrative vectors to construct lacZ fusions
AUTHOR(S): Brito, N.; Perez, M. D.; Perdomo, G.; Gonzalez, C.; Garcia-Luis, P.; Siverio, J. M.
CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Grupo del Metabolismo del Nitrogeno - Consejo Superior de Investigaciones Cientificas, Universidad de La Laguna, La Laguna, E-38206, Spain
SOURCE: Appl. Microbiol. Biotechnol. (1999), 53(1), 23-29
CODEN: AMBIDG; ISSN: 0175-7598
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A set of YEp Saccharomyces cerevisiae-based, integrative **Hansenula polymorpha** plasmids was constructed to express lacZ gene under yeast gene promoters. The HpLEU2 and HpURA3 genes were used both as markers and to target the integration of plasmids into the corresponding **H. polymorpha** genome locus. The frequency of transformation reached with these plasmids linearized either in HpLEU2 or HpURA3 was around 100 transformants per .mu.g of plasmid DNA; in all transformants checked by Southern blotting the plasmid was integrated into the genome locus corresponding to the gene plasmid marker. PCR showed that about 50% of the transformants contained more than one plasmid copy per genome. Expts. carried out using the developed plasmids to det. the strength of the gene promoters involved in nitrate assimilation in **H. polymorpha** revealed that, in the presence of nitrate, the nitrate **reductase** gene promoter (YNR1) was the strongest, followed by nitrite **reductase** (YNI1) and nitrate transporter (YNT1).

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:753607 HCAPLUS
DOCUMENT NUMBER: 130:107341
TITLE: Clustering of the YNA1 gene encoding a Zn(II)2Cys6 transcriptional factor in the yeast Hansenula polymorpha with the nitrate assimilation genes YNT1, YNI1 and YNR1, and its involvement in their transcriptional activation
AUTHOR(S): Avila, Julio; Gonzalez, Celedonio; Brito, Nelida; Siverio, Jose M.
CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Universidad de La Laguna, La Laguna, E-38206, Spain
SOURCE: Biochem. J. (1998), 336(3), 647-652
CODEN: BIJOAF; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The genes encoding the nitrate transporter (YNT1), nitrate **reductase** (YNI1) and nitrate **reductase** (YNR1) are clustered in the yeast **Hansenula polymorpha**. In order to clone, DNA sequencing of the region contg. these genes demonstrated that a novel open reading frame called YNA1 (yeast nitrate assimilation) was located between YNR1 and YNI1. The YNA1 gene encodes a protein of 529 residues belonging to the family of Zn(II)2Cys6 fungal transcriptional factors, and has the highest similarity to the transcriptional factors encoded by niiA, and to a smaller extent to nit-4, involved in the nitrate induction of the genes involved in the assimilation of this compd. in filamentous fungi. Northern blot anal. showed the presence of the YNA1 transcript in cells incubated in nitrate, nitrate plus ammonium, ammonium, and nitrogen-free media, with a decrease in its levels in those cells incubated in ammonium. In nitrate the strain .DELTA.yna1::URA3, with a disrupted YNA1 gene, neither grew nor expressed the genes YNI1, YNR1 and YNT1. In the gene cluster YNT1-YNI1-YNA1-YNR1, the four genes were transcribed independently in the YNT1 .fwdarw. YNR1 direction and the transcription start sites were detd. by primer extension.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:566359 HCAPLUS
DOCUMENT NUMBER: 129:257497
TITLE: Metabolism of methanol and xylose in a catalase-negative mutant of Hansenula polymorpha grown on combined substrates
AUTHOR(S): Agnieva, L. P.; Trotsenko, Yu. A.
CORPORATE SOURCE: Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences, Pushchino, 142292, Russia
SOURCE: Microbiology (Moscow) (1998), 67(4), 473-477
CODEN: MIBLAO; ISSN: 0026-2617
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activities of the key enzymes of methanol and xylose metab. and the ratio of the pools of reduced and oxidized glutathione (GSH/GSSG) were detd. in a catalase-neg. mutant of the methylotrophic yeast **Hansenula polymorpha** B9 (leu-,cat-) grown in continuous culture on methanol plus xylose and in fed-batch cultures on straw hydrolyzate or methanol plus straw hydrolyzate. Mutant B9 showed high alc. oxidase (AO) activity when grown on xylose or straw hydrolyzates. The addn. of methanol (0.1-1.0%) to the medium enhanced AO activity two-fold. In contrast, the activities of the key enzymes of xylose metab., xylose **reductase** and xylitol dehydrogenase, changed inversely with the methanol concn. in the medium. The activity of cytochrome c peroxidase increased at an equimolar methanol-to-xylose ratio, reverting to the initial level with increasing methanol concn. The oxidn. of most of the glutathione in response to the addn. of methanol suggests the involvement of GSH in the detoxication of hydrogen peroxide.

L15 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:568063 HCAPLUS
DOCUMENT NUMBER: 129:141340
TITLE: Nitrate regulation and the isolation of Nit- mutants in Hansenula polymorpha
AUTHOR(S): Pignocchi, Cristina; Berardi, Enrico; Cox, Brian S.
CORPORATE SOURCE: Laboratorio di Genetica Microbica, Dipartimento di

Biotecnologie Agrarie ed Ambientali, Universita degli Studi di Ancona, Ancona, I-60131, Italy
SOURCE: Microbiology (Reading, U. K.) (1998), 144(8), 2329-2330
CODEN: MPOBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hansenula polymorpha** (syn. Pichia angusta) is able to grow on nitrate as sole nitrogen source. Nitrate **reductase** (NR) assays, optimized in crude exts. from nitrate-grown cells, revealed that NR preferentially used NADPH, but also used NADH, as electron donor and required FAD for max. activity. NR activity was present in nitrate-grown and nitrite-grown cells, and was absent in cells grown in ammonium, glutamate and methylamine. Addn. of reduced nitrogen compds. to nitrate-grown cells led to loss of NR activity, even if they were added with nitrate. Under nitrogen starvation, NR activity was not obsd.; however, following growth on nitrate, NR activity is maintained in the absence of nitrate. Increases but not decreases in NR activity were dependent on protein synthesis. Conditions for chlorate selection were optimized, and Nit- (nitrate-) mutants were isolated. Some of these mutants showed reduced or absent NR activity. Sixty-one NR- mutants revealed the monogenic recessive nature of their lesions and were grouped in 10 complementation classes. These mutants will be used in gene cloning exps. aimed at identifying structural and regulatory elements involved in the first step of nitrate reqn.

L15 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:81709 HCAPLUS
DOCUMENT NUMBER: 126:136476
TITLE: The YNT1 gene encoding the nitrate transporter in the yeast **Hansenula polymorpha** is clustered with genes YNI1 and YNR1 encoding nitrite **reductase** and nitrate **reductase**, and its disruption causes inability to grow in nitrate
AUTHOR(S): Perez, M. Dolores; Gonzalez, Celedonio; Avila, Julio; Brito, Nelida; Siverio, Jose M.
CORPORATE SOURCE: Dep. Bioquim. Biol. Mol., Univ. La Laguna, La Laguna, E-38206, Spain
SOURCE: Biochem. J. (1997), 321(2), 397-403
CODEN: BIJOAF; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DNA sequencing in the phage .lambda.JA13 isolated from a .lambda. EMBL3 **Hansenula polymorpha** genomic DNA library contg. the nitrate **reductase**-(YNR1) and nitrite **reductase**-(YNI1) encoding genes revealed an open reading frame (YNT1) of 1524 nucleotides encoding a putative protein of 508 amino acids with great similarity to the nitrate transporters from Aspergillus nidulans and Chlamydomonas reinhardtii. Disruption of the chromosomal YNT1 copy resulted in inability to grow in nitrate and a significant redn. in rate of nitrate uptake. The disrupted strain is still sensitive to chlorate, and, in the presence of 0.1 mM nitrate, the expression of YNR1 and YNI1 and the activity of nitrate **reductase** and nitrite **reductase** are significantly reduced compared with the wild-type. Northern-blot anal. showed that YNT1 is expressed when the yeast is grown in nitrate and nitrite but not in ammonium soln.

L15 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:439575 HCAPLUS
DOCUMENT NUMBER: 125:159562
TITLE: The genes YNI1 and YNR1, encoding nitrite **reductase** and nitrate **reductase** respectively in the yeast **Hansenula polymorpha**, are clustered and coordinately regulated
AUTHOR(S): Brito, Nelida; Avila, Julio; Perez, Ma. Dolores; Gonzalez, Celedonio; Siverio, Jose M.
CORPORATE SOURCE: Dep. Bioquim. Biol. Mol., Univ. La Laguna, La Laguna, E-38206, Spain.
SOURCE: Biochem. J. (1996), 317(1), 89-95
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nitrite **reductase**-encoding gene YNI1 from the yeast **Hansenula polymorpha** was isolated from a Lambda EMBL3 **H. polymorpha** genomic DNA library, using as a probe a 761 bp DNA fragment from the gene of Aspergillus nidulans encoding nitrite **reductase** (niiA). An open reading frame of 3132 bp, encoding a putative protein of 1044 amino acids with high similarity with nitrite **reductases** from fungi, was located by DNA sequencing in the phages .lambda.NB5 and .lambda.JA13. Genes YNI1 and YNR1 (encoding nitrate **reductase**) are clustered, sepd. by 1700 bp. Northern blot anal. shows that expression for YNI1 and YNR1 is coordinately regulated; induced by nitrate and nitrite and repressed by sources of reduced nitrogen, even in the presence of nitrate. A mutant lacking nitrite **reductase** activity was obtained by deletion of the chromosomal copy of YNI1. The mutant does not grow in nitrate or in nitrite; it exhibits a similar level of transcription of YNR1 to the wild type, but the nitrate **reductase** enzymic activity is only about 50% of the wild type. In the presence of nitrate the .DELTA.yni1::URA3 mutant extrudes approx. 24 nmol of nitrite/h per mg of yeast (wet wt.), about five times more than the wild type.

L15 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:728147 HCAPLUS
DOCUMENT NUMBER: 123:138433
TITLE: Ethanol biotransformation into acetaldehyde by wild-type and mutant strains of the methylotrophic yeast Hansenula polymorpha
AUTHOR(S): Morez, O. M.; Kshemins'kaya, G. F.; Sibirny, A. A.
CORPORATE SOURCE: L'vov. Gos. Univ., Lvov, Ukraine
SOURCE: Mikrobiologiya (1994), 63(6), 1050-7
CODEN: MIKBA3; ISSN: 0026-3656
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Ethanol conversion into acetaldehyde by intact cells of wild-type and mutant strains of the methylotrophic yeast **Hansenula polymorpha** was studied. It was found that the mutations affecting alc. oxidase **reductase** and acetaldehyde dehydrogenase stimulate acetaldehyde accumulation. Maximal accumulation of acetaldehyde was obsd. in the mutant possessing elevated alc. oxidase activity in glucose medium. Impairment of formaldehyde dehydrogenase does not stimulate acetaldehyde accumulation.

L15 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:668739 HCAPLUS
DOCUMENT NUMBER: 123:248047
TITLE: Cloning and disruption of the YNR1 gene encoding the

nitrate **reductase** apoenzyme of the yeast **Hansenula polymorpha**

AUTHOR(S): Avila, Julio; Perez, M. Dolores; Brito, Nelida; Gonzalez, C-leonio; Rivero, Jose M.

CORPORATE SOURCE: Departamento de Bioquimica y Biologia Molecular, Universidad de La Laguna, E-38206 La Laguna, Tenerife, Canarias, Spain

SOURCE: FEBS Lett. (1990), 266(1-2), 37-42
CODEN: FEBLAL; ISSN: 0014-5793

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nitrate **reductase** gene (YNR1) from the yeast **H. polymorpha** was isolated from a lambda EMBL3 genomic DNA library. As probe a 350 bp DNA fragment synthesized by PCR from **H. polymorpha** cDNA was used. By DNA sequencing an ORF of 2,577 bp was found. The predicted protein has 859 amino acids and presents high identity with nitrate **reductases** from other organisms. Chromosomal disruption of YNR1 causes inability to grow in nitrate. Northern blot anal. showed that YNR1 expression is induced by nitrate and repressed by ammonium.

L15 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:404686 HCAPLUS
DOCUMENT NUMBER: 119:4686
TITLE: Targeting sequences of the two major peroxisomal proteins in the methylotrophic yeast Hansenula polymorpha
AUTHOR(S): Hansen, Hans; Didion, Thomas; Thiemann, Astrid; Veenhuis, Marten; Roggenkamp, Reiner
CORPORATE SOURCE: Inst. Mikrobiol., Heinrich-Heine-Univ. Duesseldorf, Duesseldorf, W-4000, Germany
SOURCE: Mol. Gen. Genet. (1992), 235(2-3), 269-78
CODEN: MGGEAE; ISSN: 0026-8925
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dihydroxyacetone synthase (DAS) and methanol oxidase (MOX) are the major enzyme constituents of the peroxisomal matrix in the methylotrophic yeast **H. polymorpha** when grown on methanol as a sole carbon source. To characterize their topogenic signals the localization of truncated polypeptides and hybrid proteins was analyzed in transformed yeast cells by subcellular fractionation and electron microscopy. The C-terminal part of DAS, when fused to the bacterial .beta.-lactamase or mouse dihydrofolate **reductase**, directed these hybrid polypeptides to the peroxisome compartment. The targeting signal was further delimited to the extreme C-terminus, comprising the sequence N-R-L-COOH, similar to the recently identified and widely distributed peroxisomal targeting signal (PTS) S-K-L-COOH in firefly luciferase. By an identical approach, the extreme C-terminus of MOX, comprising the tripeptide A-K-F-COOH, was shown to be the PTS of this protein. Furthermore, on fusion of a C-terminal sequence from firefly luciferase including the PTS, .beta.-lactamase was also imported into the peroxisomes of **H. polymorpha**. It is concluded that, besides the conserved PTS (or described variants), other amino acid sequences with this function have evolved in nature.

L15 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:510631 HCAPLUS
DOCUMENT NUMBER: 115:110631
TITLE: Methanol metabolism in a peroxisome-deficient mutant of Hansenula polymorpha: a physiological study

AUTHOR(S): Van der Klei, Ida J.; Harder, Wim; Veenhuis, Marten
CORPORATE SOURCE: Biol. Cent., Univ. Groningen, Haren, 9751 NN, Neth.
SOURCE: Arch. Microbiol. (1991), 156(1), 19-23
CODEN: AMICCW; ISSN: 0302-8933

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Methanol-utilization was studied in a peroxisome-deficient (PER) mutant of Hansenula polymorpha. In spite of the fact that in carbon-limited chemostat cultures under induced conditions the enzymes involved in methanol metab. were present at wild-type (WT) levels, this mutant is unable to grow on methanol as a sole carbon and energy source. Addn. of methanol to glucose-limited (S = 12.5 mM) chemostat cultures of the PER mutant only resulted in an increase in yield when small amts. were used (up to 22.5 mM). At increasing amts. however, a gradual decrease in cell yield was obsd. which, at 80 mM methanol in the feed, had dropped below the original value of the glucose-limited culture. This redn. in yield was not obsd. when increasing amts. of formate instead of methanol were used as supplements for the glucose-limited mutant culture and also not in WT cells, used as control in these expts. The effect of addn. of methanol to a glucose-limited PER culture was also studied in the transient state during adaptation of the cells to methanol. The enzyme patterns obtained suggested that the ultimate decrease in yield obsd. at enhanced methanol concns. was due to an inefficient methanol metab. as a consequence of the absence of peroxisomes. The absence of intact peroxisomes results in two major problems namely i) in H2O2-metab., which most probably is no longer mediated by catalase and ii) the inability of the cell to control the fluxes of formaldehyde, generated from methanol. The energetic consequences of this metab., compared to the WT situation which intact peroxisomes, are discussed.

L15 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:404131 HCAPLUS
DOCUMENT NUMBER: 115:4131
TITLE: Diacetyl reductase from Lactobacillus
INVENTOR(S): Hummel, Werner; Kula, Maria Regina; Boermann, Frank
PATENT ASSIGNEE(S): Forschungszentrum Juelich G.m.b.H., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP [illegible]	A2	19900613	EP 1989-121786	19891124
EP [illegible]	A3	19910529		
EP [illegible]	B1	19950201		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
DE [illegible]	A1	19900705	DE 1988-3840751	19881203
DK [illegible]	A	19900604	DK 1989-5842	19891019
JP [illegible]	A2	19900927	JP 1989-310841	19891201
US [illegible]	A	19911117	US 1991-715718	19910613
PRIORITY APPLN. INFO.:			DE 1988-3840751	19881203
			US 1989-447111	19891201

AB Two diacetyl reductases (mol. wt. 66,000 and 74,000, resp.), specific for the selective redn. of diacetyl into (+)-acetoin, in the presence of NADH, were obtained from L. kefir by extn. with 0.1% 2-mercaptoethanol-contg. 100 mM Tris-HCl buffer (pH 9), followed by removal of the cell fragments by selective heat denaturing at several chromatog. purifn. steps. The

optimum pH for the enzymic activity was 5, the optimum temp. 70.degree.. Stable on storage at 6.degree. and pH 5-10 resulted in 60% residual activity. Substrate specificity was also shown, i.e., for pyruvates, diacetybenzene and 1,2-naphthoquinone.

L15 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:78409 HCAPLUS
DOCUMENT NUMBER: 114:78409
TITLE: Mutants of methylotrophic yeasts **Hansenula polymorpha** with defective formaldehyde **reductase**
AUTHOR(S): Sibirnyi, A. A.; Kshevinskaya, G. P.; Ubiivovk, V. M.; Gonchar, M. V.; Kapul'tsevich, Yu. G.; Blizhnik, K. M.
CORPORATE SOURCE: A. V. Palladin Inst. Biochem., Lvov, 290005, USSR
SOURCE: Biotekhnologiya (1990), (5), 13-17
CODEN: BTKNEZ; ISSN: 0233-2758
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Mutants of methylotrophic yeasts **H. polymorpha** resistant to allyl alc. while growing in glucose-contg. medium were selected. They retain ability to grow on media contg. ethanol, glycerol or methanol. Mutant cells of the exponential growth stage possessed a substantially diminished alc. dehydrogenase activity and almost completely lacked formaldehyde **reductase** activity. When growing on methanol-contg. medium, formaldehyde **reductase** activity might be exhibited by one of alc. dehydrogenase isoenzymes. In methanol-contg. medium mutant cells in lag-stage accumulated enhanced quantities of formaldehyde thus indicating the role of formaldehyde **reductase** in regulation of formaldehyde level in cells. Accumulation of formaldehyde in cultural fluid of mutants was accompanied by drop in activity of alc. oxidase, alc. dehydrogenase, and formaldehyde dehydrogenase and lowering of ATP pool. NADH concn. in mutant cells was also lowered. Mutants did not differ from the wild-type strain in growth rate and biomass yield from methanol either upon batch or continuous cultivation. The role of formaldehyde **reductase** in methylotrophic growth is discussed.

L15 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:39026 HCAPLUS
DOCUMENT NUMBER: 114:39026
TITLE: Reactions of direct formaldehyde oxidation to carbon dioxide are nonessential for energy supply of yeast methylotrophic growth
AUTHOR(S): Sibirny, A. A.; Ubiivovk, V. M.; Gonchar, M. V.; Titorenko, V. I.; Voronovskii, A. Yu.; Kapul'tsevich, Yu. G.; Blizhnik, K. M.
CORPORATE SOURCE: A. V. Palladin Inst. Biochem., Lvov, 290005, USSR
SOURCE: Arch. Microbiol. (1990), 154(6), 566-71
CODEN: AMICCW; ISSN: 0302-8933
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutants of the methylotropic yeast Hansenula polymorpha deficient in NAD-dependent formaldehyde or formate dehydrogenases have been isolated. They were more sensitive for exogenous methanol but retained the ability for methylotrophic growth. In the medium with methanol, the growth yields of the mutant 356-8B deficient in formaldehyde dehydrogenase and of the wild-type strain were identical (0.34 g cells g methanol) under chemostat cultivation. These results indicate that enzymes of direct formaldehyde oxidn. are not indispensable for methylotrophic growth. At the same time, inhibition of the tricarboxylic acid cycle has resulted in suppression of

... media with multicarbon nonfermentable substrates, such as ..., succinate, ethanol, and dihydroxyacetone as well as with ..., but not with glucose. In expts. with the wild-type strain H. ..., it has been shown that citrate and dihydroxyacetone inhibit ... activity incorporation from 14C-methanol into CO2. The data ... that for the dissimilation of methanol and the supplying of ... for methylotrophic growth, the functioning of tricarboxylic acid ... reactions as opposed to those of direct formaldehyde oxidn. is ...

L15 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:524145 HCAPLUS
DOCUMENT NUMBER: 113:124145
TITLE: Utilization of xylose and xylitol by yeasts
AUTHOR(S): Nishise, Hiroshi; Kajiki, Yuko; Matsuo, Ryutaro
CORPORATE SOURCE: Koshien Univ., Takarazuka, 665, Japan
SOURCE: Koshien Daigaku Kiyo, A (1990), Volume Date 19-9, ..., 9-15
CODEN: KOKAEH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hansenula polymorpha**, a methanol-utilizing yeast, grew ... xylose and xylitol. This strain grown on xylose, xylitol and glycerol ... the activity of NAD+-dependent xylitol dehydrogenase. Three ... of Candida utilis grew on xylose, but not on xylitol. They did ... the activity xylose isomerase. The strain MF 101, isolated from ... grew on xylose and xylitol, showed activities of xylose **reductase** and xylitol dehydrogenase.

L15 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:215157 HCAPLUS
DOCUMENT NUMBER: 112:215157
TITLE: Methanol-dependent production of dihydroxyacetone and glycerol by mutants of the methylotrophic yeast Hansenula polymorpha blocked in dihydroxyacetone kinase and glycerol kinase
AUTHOR(S): De Koning, W.; Weusthuis, R. A.; Harder, W.; Dijkhuizen, L.
CORPORATE SOURCE: Dep. Microbiol., Univ. Groningen, Haren, NL-9751 NN, Neth.
SOURCE: Appl. Microbiol. Biotechnol. (1990), ... , 693-8
CODEN: AMBIDG; ISSN: ...
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Various factors controlling dihydroxyacetone (DHA) and glycerol prodn. from methanol by resting cell suspensions of a mutant of **H. polymorpha**, blocked in DHA kinase and glycerol kinase, were ... The presence of methanol (150 mM) and an addnl. substrate (... , w/v) to replenish the xylulose-5-phosphate required for the ... reaction (DHA synthase) was essential for significant triose ... by this double mutant. A no. of sugars were tested as addnl. ... and C5 sugars gave the highest triose accumulation (ca. 20 mM ... 48 h). Glucose was the poorest addnl. substrate and triose prodn. ... started after its exhaustion, which occurred in the first few hours. ... sugars were metabolized at a much lower rate and accumulation of ... began right at the start of the expts. and gradually increased ... time. The prodn. rate of total trioses increased, and the relative ... of glycerol diminished with higher oxygen supply rates. The data ... that conversion of DHA into glycerol, catalyzed by reduced ... adenine dinucleotide (NADH)-dependent DHA **reductase**, is

[illegible] regulated via intracellular NADH levels. Further support for this [illegible] was obtained in expts. with antimycin A, an inhibitor of the [illegible] transport chain. Addn. of higher amts. of methanol and xylose, either by increasing the initial concns. or by repeated addn. of these substrates, resulted in considerably enhanced productivity and a switch [illegible] glycerol formation. After reaching a level of approx. 25 mM the [illegible] remained const. while the glycerol level gradually increased [illegible]. After an incubation period of 3-4 h, a total of 3.9 M methanol and 1.6 M xylose had been converted, which resulted in accumulation of [illegible] moles, mostly glycerol.

L15 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:611339 HCAPLUS
DOCUMENT NUMBER: 109:211339
TITLE: Properties of enzymes which reduce dihydroxyacetone and related compounds in Hansenula polymorpha CBS 4732
AUTHOR(S): Verduyn, Cornelis; Breedveld, Guido J.; Dijkhuizen, Henk; Scheffers, W. Alexander; Van Dijken, Johannes P.
CORPORATE SOURCE: Dep. Microbiol. Enzymol., Delft Univ. Technol., Delft, 2628 BC, Neth.
SOURCE: Yeast (1988), 4(1), 117-26
CODEN: YESTE3; ISSN: 0749-503X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **H. polymorpha** CBS 4732 grown on a variety of substrates contained very high activities of enzymes catalyzing the NADH-linked redn. of dihydroxyacetone, acetoin, diacetyl, acetol, methylglyoxal, and acetone. The enzymes catalyzing these redns. were purified and their kinetic properties are described. Three different enzymes were responsible for the above-mentioned activities; dihydroxyacetone **reductase**, acetone **reductase**, and diacetyl reductase. So far, the physiol. function of dihydroxyacetone **reductase** and acetone **reductase** is obscure. The kinetic properties of dihydroxyacetone **reductase** and the regulation of the synthesis of this enzyme suggest that it does not function as a glycerol dehydrogenase.

L15 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:614645 HCAPLUS
DOCUMENT NUMBER: 107:214645
TITLE: Glycerol metabolism in the methylotrophic yeast Hansenula polymorpha: phosphorylation as the initial step
AUTHOR(S): De Koning, W.; Harder, W.; Dijkhuizen, L.
CORPORATE SOURCE: Lab. Microbiol., Univ. Groningen, Haren, NL-9751 NN, Neth.
SOURCE: Arch. Microbiol. (1987), 148(4), 314-20
CODEN: AMICCW; ISSN: 0302-8933
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In H. polymorpha glycerol is metabolized via glycerol kinase and NAD(P)-independent glycerol 3-phosphate (G3P) dehydrogenase, enzymes which [illegible] were reported to be absent in this methylotrophic yeast. Activity of glycerol kinase was readily detectable when cell-free exts. were incubated at pH 7-8 with glycerol, ATP, and Mg2+ and a discontinuous assay for G3P formation was used. This glycerol kinase activity could be [illegible] from dihydroxyacetone (DHA) kinase activity by ion exchange [illegible]. Glycerol kinase showed relatively low affinities for glycerol (apparent Km = 1.0 mM) and ATP (apparent Km = .5 mM) and was not active [illegible] other substrates tested. No inhibition by fructose 1,6-bisphosphate

... was also obsd. Both NAD-dependent and NAD(P)-independent G3P dehydrogenases were present. Glucose partly repressed synthesis of glycerol kinase and NAD(P)-independent G3P dehydrogenase, but compared to several other non-repressing C sources no clear induction of these enzymes by glycerol was apparent. Among glycerol-neg. mutants of H. polymorpha strain 15 (DHA kinase-neg. mutant), strains blocked in either glycerol kinase or membrane-bound G3P dehydrogenase were identified. Crosses between representatives of the latter mutants and wild type resulted in ... recombination of, among others, prototrophs which had regained DHA kinase activity but were still blocked in the membrane-bound G3P dehydrogenase. These strains, employing the oxidative pathway, were only able to grow very slowly on glycerol mineral medium.

L15 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:436369 HCAPLUS
DOCUMENT NUMBER: 107:36369
TITLE: Regulation of methanol metabolism in the yeast Hansenula polymorpha. Isolation and characterization of mutants blocked in methanol assimilatory enzymes
AUTHOR(S): De Koning, W.; Gleeson, M. A. G.; Harder, W.; Kiykhuizen, L.
CORPORATE SOURCE: Dep. Microbiol., Univ. Groningen, Haren, NL-9751 NN, Neth.
SOURCE: Arch. Microbiol. (1987), 147(4), 376-82
CODEN: AMICCW; ISSN: 0302-8933
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study of enzyme profiles in **H. polymorpha** grown on various carbon substrates revealed that the synthesis of the methanol dissimilatory and assimilatory enzymes is regulated in the same way, namely by catabolite repression and induction by methanol. Mutants of **H. polymorpha** blocked in dihydroxyacetone (DHA) synthase (strain 70M) or DHA kinase (strain 17 B) were unable to grow on methanol, which confirmed the important role attributed to these enzymes in the biosynthetic xylulose monophosphate (XuMP) cycle. Both mutant strains were still able to metabolize methanol. In the DHA kinase-neg. strain 17 B, this resulted in accumulation of DHA. Although DHA kinase is thought to be involved in DHA and glycerol metab. in methylotrophic yeasts, strain 17 B was still able to grow on glycerol at a rate similar to that of the wild type. DHA, on the other hand, only supported slow growth of this mutant when relatively high concns. of this compd. were provided in the medium. This slow, but definite, growth of strain 17 B on DHA was not based on the reversible DHA synthase reaction but on conversion of DHA into glycerol, a reaction catalyzed by DHA **reductase**. The subsequent metab. of glycerol in strain 17 B and in wild-type **H. polymorpha**, however, remains to be elucidated.

L15 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:576091 HCAPLUS
DOCUMENT NUMBER: 89:176091
TITLE: Dihydroxyacetone: an intermediate in the assimilation of methanol by yeasts
AUTHOR(S): Van Dijken, J. P.; Harder, W.; Beardsmore, A. J.; Quayle, J. R.
CORPORATE SOURCE: Biol. Cent., Univ. Groningen, Haren, Neth.
SOURCE: FEMS Microbiol. Lett. (1978), 4(2), 97-102
CODEN: FMLEDY; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Methanol assimilation was investigated in 2 yeast strains, **Hansenula**

polymorpha CBS 4732 and Candida boidinii CBS 5777. Ribulose [illegible] carboxylase, malyl-CoA lyase, hydroxypyruvate **reductase**, glycerate kinase, and isocitrate lyase were not detected in cell-free exts. of MeOH-grown **H. polymorpha** , indicating that MeOH is not assimilated via the Calvin cycle of the serine pathway. During the 1st 4[illegible] s of incubation with MeOH-14C, [illegible]% of the isotype fixed was present in phosphorylated compds. Following dephosphorylation of these compds., followed by chromatog. and autoradiog. anal., showed them to consist mainly of phosphates of glucose, fructose, and mannose, with fructose phosphate as precursor of the glucose and mannose phosphates. Appreciable activities of hexulose phosphate synthase were not detected in cell-free exts. of MeOH-grown **H. polymorpha** and C. boidinii, and hexulose phosphate isomerase activity was very low indicating the absence of the ribulose monophosphate pathway. 6-Phosphofructokinase also was not involved in the assimilation of MeOH by these organisms. The induction of a triokinase and of fructose 1,6-diphosphatase during growth of these organisms on MeOH fulfills part of the requirement of a dihydroxyacetone pathway with the substrate specificity of the triokinase indicating that dihydroxyacetone may be the physiol. substrate for this enzyme.

=> d ibib abs 1

L27 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:59936 HCAPLUS
DOCUMENT NUMBER: 130:192833
TITLE: Rapid alcohol determination in plasma and urine by **column** liquid chromatography with biosensor detection
AUTHOR(S): Liden, Helena; Vijayakumar, A. R.; Gorton, Lo; Marko-Varga, Gyorgy
CORPORATE SOURCE: Department of Analytical Chemistry, Lund University, Lund, 221 00, Swed.
SOURCE: J. Pharm. Biomed. Anal. (1998), 17(6,7), 1111-1128
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enzyme based amperometric biosensor used as a selective and sensitive detection unit in **column** liq. chromatog. for the detn. of ethanol and methanol in biol. fluids such as plasma and urine is described. The reagentless enzyme electrode is based on the co-immobilization of alc. oxidase and horseradish peroxidase in carbon paste. The selectivity of the biosensor was found to vary when four various alc. oxidase enzyme **prepns.** from Candida boidinii, Pichia pastoris, and **Hansenula polymorpha** were used in the biosensors described. High sensitivity could be obtained for a no. of alcs., org. acids, and aldehydes. Optimization regarding the sensitivity and selectivity of the four alc. oxidase co-immobilized biosensors are outlined. A fast and reliable liq. chromatog. sepn. system with a PLRP-S polymer based sepn. **column** used with a phosphate buffer as the mobile phase was optimized using the best biosensor which was based on alc. oxidase from P. pastoris and which showed the highest turnover rate for alcs., as the detector for the detn. of ethanol and methanol in human urine and plasma samples. The selectivity and stability of the biosensor were retained by working at an applied potential of - 50 mV vs. Ag/AgCl, the optimal operational potential, and by the casting of a protective membrane on the electrode surface. High selectivity of the enzyme electrode was also found towards other easily oxidizable interfering species normally present in biol. fluids. It was found that stable and reliable detns. of ethanol and methanol in plasma and urine could be performed with only a simple diln. and centrifugation step prior to injection into the liq. chromatog. system. An anal. time of 4 min was required for the assay, with a sample throughput of 13 samples h-1.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 2

L27 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:296738 HCAPLUS
DOCUMENT NUMBER: 120:296738
TITLE: Production, purification and immobilization of inulinase from Kluyveromyces fragilis
AUTHOR(S): Gupta, Anil K.; Singh, Davinder Pal; Kaur, Narinder; Singh, Rangil
CORPORATE SOURCE: Dep. Biochem., Punjab Agric. Univ., Ludhiana, 141004, India
SOURCE: J. Chem. Technol. Biotechnol. (1994), 59(4), 377-85
CODEN: JCTBED; ISSN: 0268-2575
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kluyveromyces fragilis (NCIM 3217), Kluyveromyces marxianus (NCIM 3231), **Hansenula polymorpha** (NCIM 3377), Pichia fermentans (NCIM 3408), Pichia polymorpha (NCIM 3419) and Debaryomyces castellii (NCIM 3446) were grown on an inulin-based growth medium. Only K. fragilis produced extracellular inulinase with a max. after 36 h of growth at 25-27.degree.. Sucrose and fructose were weak inducers of inulinase as compared to inulin whereas with glucose the inulinase level was minimal. An aq. ext. of chicory roots contg. 1% fructan was a better carbon source than inulin and peptone was the best nitrogen source for the prodn. of inulinase. The max. yield of inulinase was about 7 units cm-3 of medium. The invertase to inulinase ratio of 10 in the culture filtrate was reduced to 1.6 on purifying inulinase by etnanol **pptn.** followed by chromatog. on Sephadex G-200, DEAE-cellulose and CM-cellulose **columns.** Using this purifn. procedure, inulinase was purified 26-fold. With inulin as substrate, the shape of the velocity curve was nearer to a sigmoidal pattern whereas with sucrose the curve was hyperbolic. The mol. wt. of inulinase was detd. as 250 +/- 10 kDa. The crude and purified inulinase **prepns.** did not release sucrose or oligosaccharides from inulin, indicating that the enzyme has primarily exo-inulinase activity. Using the metal-link chelation method, 40% of inulinase was immobilized on cellulose. Max. activity of crude, purified and immobilized inulinase **prepns.** was obsd. at 55.degree.. The half-life of immobilized inulinase at 25.degree. was 5 days.

=> d ibib abs 3

L27 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:71580 HCAPLUS
DOCUMENT NUMBER: 110:71580
TITLE: Purification and properties of alcohol oxidase from Hansenula polymorpha P-5
AUTHOR(S): Chen, Hwei Fen; Chen, Trann Jin; Fang, Hung Yuan
CORPORATE SOURCE: Refin. Manuf. Res. Cent., Chin. Pet. Co., Taiwan
SOURCE: Chung-kuo Nung Yeh Hua Hsueh Hui Chih (1988), 26(3), 287-301
CODEN: CKNHAA; ISSN: 0578-1736
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The alc. oxidase was extd. from MeOH-grown yeast **H. polymorpha** P-5, and is stable in 50 mM phosphate buffer at 7.5. The specific activity of crude ext. is 0.33 .mu.moles MeOH oxidized min-1. (mg protein)-1; the activity in Tris-HCl buffer is only 70% that in Na phosphate buffer. Cl- is a reversible inhibitor of the enzyme. Alc. oxidase is also inhibited by .beta.-mercaptoethanol. The enzyme shows a broad optimum pH range (6.5-10.0), and it is unstable at lower pH. If it was incubated at 45.degree. for 30 min, the activity increased .ltoreq.170%. Almost all activity could be retained after being stored at 10.degree. for 2 days, whereas if stored at 55.degree. for 5 h or frozen below 0.degree. for 18 h, the activity was lost 83 or 93%, resp. By the use of 40-55% (NH4)2SO4 **fractionation**, Sephacryl S-300 gel filtration, DEAE-Sephacel ion exchange chromatog., Sephadex G-25 **desalting**, and Bio-Gel HTP chromatog., the alc. oxidase was purified 10-fold with 35.8% yield. The purified enzyme **prepn.** showed 2 bands on polyacrylamide disc gel electrophoresis. The major one had a mol. wt. of 620,000 and the minor one had a larger mol. wt. The purified enzyme shows absorption peaks in the visible region 373 and 458 nm with a shoulder at 396 nm. The enzyme contains noncovalently bound FAD as its prosthetic group.

=> d 1r1b abs 4

L27 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:586106 HCAPLUS
DOCUMENT NUMBER: 109:186106
TITLE: Methanol peroxidation by alcohol oxidase from methylotrophic yeasts
AUTHOR(S): Sibirnyi, A. A.; Ubiivovk, V. M.; Ksheminskaya, G. P.
CORPORATE SOURCE: A. V. Palladin Inst. Biochem., Lvov, USSR
SOURCE: Biokhimiya (Moscow) (1988), 53(6), 936-45
CODEN: BIOHAO; ISSN: 0006-297X
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB H2O2 markedly stimulated the synthesis of formaldehyde from MeOH in cell-free exts. of **Hansenula polymorpha**. This stimulation did not depend on the peroxidase properties of catalase, since it was possible to sep. the peroxidase and catalase activities. Purified **prepns.** of alc. oxidases of **H. polymorpha** and Candida boidinii possessed the methanol peroxidase activity. The reaction mixt. used for the detn. of the methanol peroxidase activity under aerobic conditions contained the enzyme (.ltoreq.1 units/mg protein) and high concns. of MeOH (.gtoreq.100 mM). Anal. of methanol peroxidase properties of alc. oxidase under anaerobic conditions revealed that the maximal activity was obsd. at 15-20 mM H2O2. The dependence of the peroxidase activity on MeOH concn. was characterized by **satn.** kinetics (Km = 2.6 mM); the pH optimum was 7.5. Methanol peroxidase did not utilize std. substrates for heme-contg. peroxidases (e.g., pyrogallol, o-dianisidine, benzidine, 3,3-diaminobenzidine). EtOH competitively inhibited MeOH peroxidn. (Ki = 15 mM). Ferricyanide, methylene blue, phenazine methosulfate and cytochrome c as well as org. peroxide and tert-Bu peroxide did not substitute for O2 or H2O2 as electron acceptors during MeOH oxidn.

=> d ibib abs 5

L27 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:73828 HCAPLUS
DOCUMENT NUMBER: 108:73828
TITLE: Process for preparing a catalase-free oxidase with a catalase-free oxidase-containing yeast
INVENTOR(S): Giuseppin, Marco Luigi Federico
PATENT ASSIGNEE(S): Unilever N. V., Neth.; Unilever PLC
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 244907	A1	19871021	EP 1987-201055	19870605
EP 244907	B1	19901017		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
AT 58169	E	19901115	AT 1987-201055	19870605
JP 63137674	A2	19880609	JP 1987-168499	19870706
JP 03065753	B4	19911014		

PRIORITY APPLN. INFO.: NL 1986-2978 19861124
EP 1987-201055 19870605

AB An oxidase or oxidase-contg. compn. free of catalase can be **prepd**. by aerobic fermn. of catalase-neg. yeast in the presence of an inducer (of the oxidase) if a 2nd C source is present, the molar ratio of inducer: 2nd C source being adjusted to prevent harmful effects to the yeast or oxidase by oxidn. of the inducer. **Hansenula polymorpha** ATCC 46059 was grown on a medium contg. MeOH and glucose in a molar ratio of 1.15. With respect to the wild-type strain cultured on MeOH/glucose, this mutant displayed 52-62% methanol oxidase expression under optimal conditions. The oxidase could be **pptd.** with 65% **satd.** (NH4)2SO4. It was stable at room temp., and contained no catalase activity.

=> d ibib ab 6

L27 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:65500 HCAPLUS
DOCUMENT NUMBER: 104:65500
TITLE: Dihydroxyacetone synthase is localized in the peroxisomal matrix of methanol-grown Hansenula polymorpha
AUTHOR(S): Douma, Annerie C.; Veenhuis, Marten; De Koning, Wim; Evers, Melchior; Harder, Wim
CORPORATE SOURCE: Dep. Microbiol., Univ. Groningen, Haren, NL-9751 NN, Neth.
SOURCE: Arch. Microbiol. (1985), 143(3), 237-43
CODEN: AMICCW; ISSN: 0302-8933
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The subcellular localization of dihydroxyacetone synthase (DHAS) in the methylotrophic yeast **H. polymorpha** was studied by various biochem. and immunocytochem. methods. After cell **fractionation** involving differential and sucrose **gradient** centrifugation of protoplast homogenates **prepd.** from MeOH-grown cells, DHAS cosedimented with the peroxisomal enzymes alc. oxidase and catalase. Electron microscopy of this **fraction** showed that it contained mainly intact peroxisomes, whereas SDS-polyacrylamide gel electrophoresis revealed 2 major protein bands (75 and 78 kilodaltons) which were identified as alc. oxidase and DHAS, resp. The localization of DHAS in peroxisomes was further established by immunocytochem. After immune Au staining carried out on ultrathin sections of MeOH-grown **H. polymorpha** using DHAS-specific antibodies, labeling was confined to the peroxisomal matrix.

=> d ibib abs hitstr 1

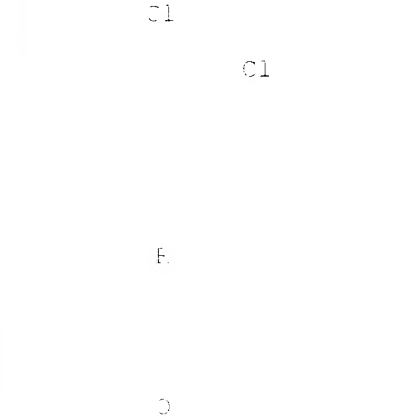
L31 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:31804 HCAPLUS
DOCUMENT NUMBER: 132:236856
TITLE: Efficient Kinetic Resolution in the Asymmetric Hydrosilylation of Imines of 3-Substituted Indanones and 4-Substituted Tetralones
AUTHOR(S): Yun, Jaesook; Buchwald, Stephen. L.
CORPORATE SOURCE: Department of Chemistry, Massachusettes Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: J. Org. Chem. (2000), 65(3), 767-774
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:236856

AB Kinetic resoln. of the N-methylimines of 3-substituted indanones and 4-substituted tetralones could be accomplished by hydrosilylation with a chiral titanocene catalyst. N-Methylimines of 4-substituted tetralones were resolved to yield, after hydrolysis of the unreacted starting materials, ketones with high ee's and the amine products with high diastereomeric and enantiomeric purity. The utility of this process was demonstrated in the synthesis of sertraline.

IT **155748-61-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)

RN 155748-61-1 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 2

L31 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:[illegible] HCAPLUS
DOCUMENT NUMBER: 131:[illegible]
TITLE: Process for the cis-selective catalytic hydrogenation of cyclohexylidenamines
INVENTOR(S): Steiner, Heinz; Benz, Markus; Jalett, Hans-Peter; Thommen, Marc
PATENT ASSIGNEE(S): Ciba Specialty Chemicals Holding Inc., Switz.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO [illegible]	A1	[illegible]	WO 1999-EP1696	19990316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU [illegible]	A1	[illegible]	AU [illegible]	[illegible]
EP [illegible]	A1	[illegible]	EP [illegible]	[illegible]
R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE				
US [illegible]	B1	20010515	US 2000-646311	20001014
PRIORITY APPLN. INFO.:			CH [illegible]	A [illegible]
			WO [illegible]	W [illegible]

OTHER SOURCE(S): CASREACT 131:[illegible]; MARPAT 131:[illegible]
AB A process for the cis-selective prepn. of cyclic amines of the sertraline type by reductive alkylation of cyclic imines or of their precursors and catalytic hydrogenation in the presence of copper-contg. catalysts is described. E.g., a Ba-doped copper chromite catalyst catalyzed hydrogenation of 4-(3,4-dichlorophenyl)-1-methylimino-1,2,3,4-tetrahydronaphthalene to give 4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthylamine (95:5 cis:trans).
IT **79560-19-3**
RL: RCT (Reactant)
(cis-selective catalytic hydrogenation of cyclohexylidenamines)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

C1

C1

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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D IND 1

L31 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
CC 21-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
ST kinetic resoln asym hydrosilylation imine; indanone imine asym hydrosilylation kinetic resoln; tetralone imine asym hydrosilylation kinetic resoln; titanocene asym hydrosilylation imine; safety asym hydrosilylation imine workup
IT Safety
(in workup of asym. hydrosilylation of imines)
IT Resolution (separation)
(kinetic; in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)
IT Hydrosilylation
(**stereoselective**; kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)
IT Hydrosilylation catalysts
(**stereoselective**; titanocene complex for imines of 3-substituted indanones and 4-substituted tetralones)
IT 178177-94-9 214361-86-1
RL: CAT (Catalyst use); USES (Uses)
(kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)
IT 74-89-5, Methylamine, reactions 107-10-8, Propylamine, reactions 694-53-1, Phenylsilane 6072-57-7, 3-Methyl-1-indanone
RL: RCT (Reactant)
(kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)
IT 261776-31-3P 261776-33-4P 261776-34-5P 261776-35-6P 261776-36-7P
261776-37-8P 261776-38-9P 261776-39-0P 261776-40-3P 261776-41-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)
IT 769-14-2P 14578-68-3P 16619-72-7P 50438-03-4P 50438-04-5P
82759-03-3P 79617-96-2P, Sertraline 79617-98-4P 79645-15-1P
96946-44-3P 98213-39-9P **155748-61-1P** 261776-42-5P
261776-43-6P 261776-44-7P 261776-45-8P 261776-46-9P 261776-47-0P
261776-48-1P 261776-49-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(kinetic resoln. in asym. hydrosilylation of imines of 3-substituted indanones and 4-substituted tetralones)

=> D IND 2

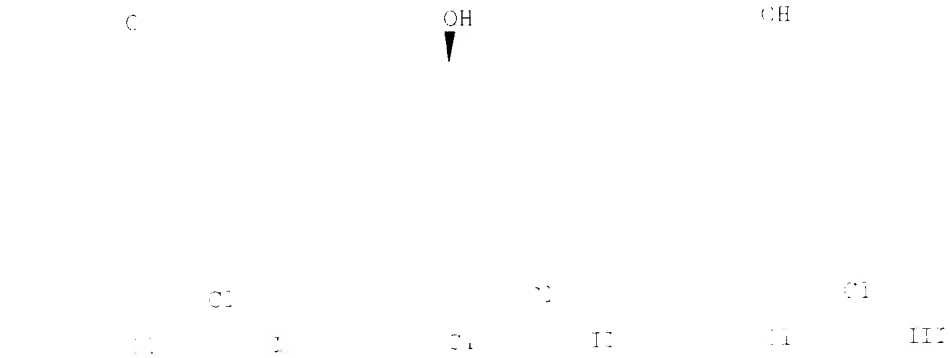
L31 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
IC ICM C07C209-52
CC 24-5 (Alicyclic Compounds)
ST naphthylamine dichlorophenyl **stereoselective** prepn; copper catalyst hydrogenation cyclohexylidenamine
IT Hydrogenation
Stereochemistry
(cis-selective catalytic hydrogenation of cyclohexylidenamines)
IT Hydrogenation catalysts
(cis-selective hydrogenation of cyclohexylidenamines in presence of copper-contg. catalysts)
IT 11104-65-7, Chromium copper oxide 39320-46-2, Barium chromium copper oxide (Ba).03Cr0.17Cu0.15O0.65 56450-21-6, Aluminum copper zinc oxide 163150-32-1, CU 0890P
RL: CAT (Catalyst use); USES (Uses)
(cis-selective catalytic hydrogenation of cyclohexylidenamines)
IT **79560-19-3** 79560-20-6 209473-00-7
RL: RCT (Reactant)
(cis-selective catalytic hydrogenation of cyclohexylidenamines)
IT 79617-89-3P 244223-39-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(cis-selective catalytic hydrogenation of cyclohexylidenamines)

=> d ibib abs hitstr IND 3

L31 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:761816 HCAPLUS
DOCUMENT NUMBER: 123:169379
TITLE: Process for preparing a chiral tetralone, useful as an intermediate for sertraline
INVENTOR(S): Quallich, George J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511209	A1	19950608	WO 1994-IB263	19940902
W: CA, FI, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2176500	AA	19950608	CA 1994-2176500	19940902
EP 731795	A1	19960918	EP 1994-926167	19940902
EP 731795	B1	19971029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09506340	T2	19970624	JP 1994-511276	19940902
AT 159709	E	19971115	AT 1994-926167	19940902
ES 2109484	T3	19980116	ES 1994-926167	19940902
FI 9602309	A	19960605	FI 1996-2309	19960604
US 5750794	A	19980512	US 1996-652489	19960529
PRIORITY APPLN. INFO.:			US 1993-159156	19931130
			WO 1994-IB263	19940902

OTHER SOURCE(S): CASREACT 123:169379; MARPAT 123:169379
GI



AB A process for prepg. the chiral ketone (4S)-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone [(S)-I; dichlorophenyl group .beta.], an intermediate for the antidepressant sertraline, is disclosed. Racemic ketone (.+-.)-I is is asym. reduced with chiral reducing agents, esp. oxazaborolidines, to produce a mixt. of cis and trans alcs., i.e., either II or III. These novel, diastereomeric alc. intermediates are sepd., and the (4S)-stereoisomer is oxidized to give (S)-I. For example, BH3.SMe2 in

THF was added to a THF soln. of (1S,2R)-(+)-erythro-2-amino-1,2-diphenylethanol to give an asym. reducing agent. Then, 5.0 g (.+-.)-I was added, and the mixt. was stirred and worked up, to give 5.01 g mixt. of cis- and trans-II, which was sepd. by chromatog. Oxidn. of 160 mg cis-II with pyridinium chlorochromate (PCC) in CH2Cl2 gave 118 mg (S)-I with stereog. 95% enantiomeric excess (ee). Alternatively, redn. of (.+-.)-I with either of 2 other asym. reagents gave III, the trans isomer of which gave (S)-I with 56% and 47% ee. Oxidn. of the unused isomers of II and III with PCC gave (R)-I, which was racemized by bases such as KOBu-tert in THF to give, e.g., 95% (.+-.)-I.

IT **79836-44-5P**, (.+-.)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and asym. redn.; asym. redn. of tetralone deriv.)

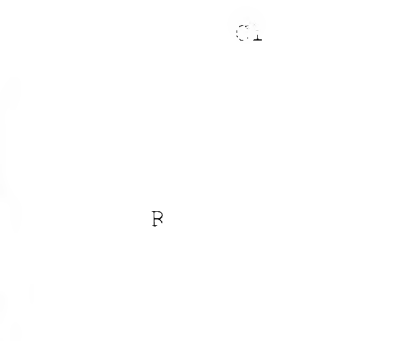
RN 79836-44-5 HCAPLUS

IT **155748-61-1P**, (4R)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn.; asym. redn. of tetralone deriv.)

RN 155748-61-1 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **124379-29-9P**, (4S)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chiral tetralone deriv. as sertraline intermediate)

RN 124379-29-9 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

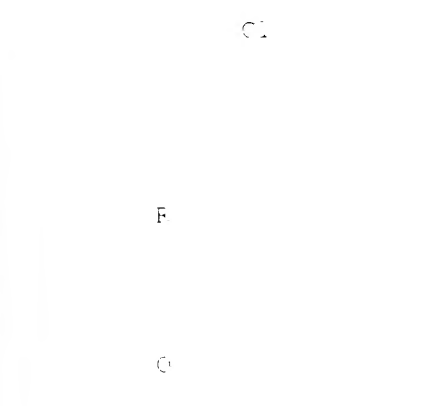
Absolute stereochemistry. Rotation (+).

IC ICM C07B053-00
ICS C07C049-143; C07C035-27; C07C045-30; C07C043-697
CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
ST tetralone dichlorophenyl chiral prepn intermediate sertraline; asym redn tetralone oxazaborolidine
IT Antidepressants
Asymmetric synthesis and induction
(prepn. of chiral tetralone deriv. as sertraline intermediate)
IT Reduction
(**stereoselective**, asym. redn. of tetralone deriv.)
IT **79836-44-5P**, (4R)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and asym. redn.; asym. redn. of tetralone deriv.)
IT **155748-61-1P**, (4R)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone 167026-37-1P 167026-40-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn.; asym. redn. of tetralone deriv.)
IT **124379-29-9P**, (4S)-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of chiral tetralone deriv. as sertraline intermediate)
IT 79617-96-2P, Sertraline
RL: PRU (Preparation, unclassified); PREP (Preparation)
(prepn. of chiral tetralone deriv. as sertraline intermediate)
IT 167026-38-2P 167026-39-3P
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation)
(recycled byproduct; asym. redn. of tetralone deriv.)
IT 23364-44-5, (1S,2R)-(+)-erythro-2-Amino-1,2-diphenylethanol
RL: RCT (Reactant)
(reducing agent precursor; asym. redn. of tetralone deriv.)
IT 112022-81-8, (S)-Tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaborole 112246-73-8, (+)-B-Chlorodiisopinocampheylborane
RL: RCT (Reactant)
(reducing agent; asym. redn. of tetralone deriv.)

=> d ibib abs hitstr IND 4

L21 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:680354 HCAPLUS
DOCUMENT NUMBER: 121:280354
TITLE: A catalytic enantioselective synthetic route to the important antidepressant sertraline
AUTHOR(S): Corey, E. J.; Gant, Thomas G.
CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Tetrahedron Lett. (1994), 35(30), 5373-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:280354
AB An efficient catalytic enantioselective synthesis of the important antidepressant sertraline is described.
IT **155748-61-1**
RL: PRP (Properties)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
RN 155748-61-1 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **124379-29-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

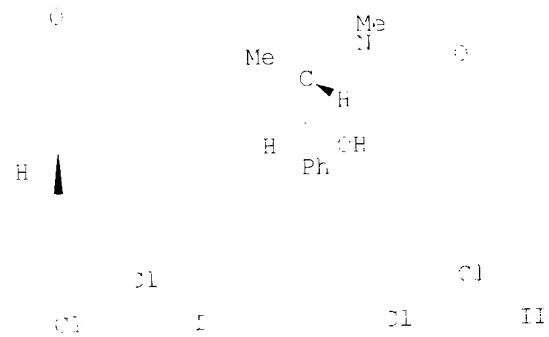
CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 63
ST enantioselective synthesis sertraline
IT Asymmetric synthesis and induction
(catalytic enanticselective synthetic route to the important antidepressant sertraline)
IT Ring closure and formation
(cyclopropanation, **stereoselective**, catalytic enantioselective synthetic route to the important antidepressant sertraline)
IT 154975-39-0
RL: CAT (Catalyst use); USES (Uses)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
IT **155748-61-1**
RL: PRP (Properties)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
IT 100-42-5, Styrene, reactions 20555-91-3, 3,4-Dichlorophenyl iodide 119987-01-2
RL: RCT (Reactant)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
IT **124379-29-9P** 147255-16-1P 153062-73-8P 156723-71-3P 158800-59-0P 158800-60-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)
IT 79617-96-2, Sertraline
RL: SPN (Synthetic preparation); PREP (Preparation)
(catalytic enantioselective synthetic route to the important antidepressant sertraline)

=> d ibib abs hitstr IND 5

L31 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:559910 HCAPLUS
DOCUMENT NUMBER: 119:159910
TITLE: Process for preparing (4S)-4-(3,4-dichlorophenyl)-3,4-dihydro-1 (2H)-naphthalenone
INVENTOR(S): Quallich, George J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5196607	A	19930323	US 1992-837012	19920214

OTHER SOURCE(S): CASREACT 119:159910
GI



AB The key step in the overall 8-step prepn. of the title compd. (I) involves **stereoselective** Grignard phenylation of chiral propenamide II (derived from L-ephedrine + 3,4-dichlorocinnamoyl chloride), affording (after hydrolysis) (3R)-(3,4-Cl2C6H3)CHPhCH2CO2H (III). The subsequent procedure involves esterification of III, ester redn. to alc., chlorination of the alc., cyanation of the Pr chloride to (4R)-(3,4-Cl2C6H3)CHPhCH2CH2CN, hydrolysis, acid chloride formation, and Friedel-Crafts cyclization to I (in 79:21 enantiomeric ratio, or 58% optical purity).

IT **124379-29-9P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. of)

RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IC ICM C07C045-41
ICS C07C045-46
NCL 568317000
CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 63
ST sertraline intermediate asym synthesis; naphthalenone dichlorophenyldihydro asym synthesis; **stereoselective** Grignard phenylation propenamide
IT Asymmetric synthesis and induction
(of (dichlorophenyl)dihydronaphthalenone)
IT Grignard reaction
stereoselective, of phenylmagnesium chloride with chiral amide derived from ephedrine and dichlorocinnamoyl chloride)
IT 10554-12-6, 3,4-Dichlorocinnamyl chloride
RL: RCT (Reactant)
(amidation of, with ephedrine)
IT 299-42-3, L-Ephedrine
RL: RCT (Reactant)
(amidation with, of dichlorocinnamyl chloride)
IT 7446-70-0, Aluminum chloride (AlCl3), uses
RL: CAT (Catalyst use); USES (Uses)
(catalysts, for Freidl-craft cyclization in isometric synthesis of (dichlorophenyl)dihydronaphthalenone)
IT 17499-13-9, 1,4,7,10,13,16-Hexaoxacyclooctadecane
RL: CAT (Catalyst use); USES (Uses)
(catalysts, for cyanation of (dichlorophenyl)phenylpropyl chloride enantiomer)
IT 603-35-0, Triphenylphosphine, reactions
RL: RCT (Reactant)
(chlorination with carbon tetrachloride and, of dichlorophenyl)phenylpropanol enantiomer)
IT 56-23-5, Carbon tetrachloride, reactions
RL: RCT (Reactant)
(chlorination with triphenylphosphine and, of dichlorophenyl)phenylpropenyl enantiomer)
IT 16853-85-3, Lithium aluminum hydride
RL: RCT (Reactant)
(ester redn. with, in asym. synthesis of (dichlorophenol)dihydronaphthalene)
IT 67-56-1, Methanol, reactions
RL: RCT (Reactant)
(esterification reaction of, in prepn. of (dichlorophenyl)dihydronaphel

ephedrine)

IT 149621-65-5P
RL: PRT (Reactant); PREP (Preparation)
(formation and Friedel-Crafts cyclization of)

IT 149621-61-1P
RL: PRT (Reactant); PREP (Preparation)
(formation and hydrolysis of)

IT 147281-16-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Friedel-Crafts cyclization of, vs chloride)

IT 149712-64-1P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and chlorination of)

IT 149621-62-2P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyanation of)

IT 149712-16-1P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of)

IT 149621-64-4P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

IT 149621-63-3P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT 149621-60-0P
RL: PRT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **stereoselective** reaction of, with phenylmagnesium chloride)

IT 151-50-8, Potassium cyanide (K(CN) **124379-29-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 100-59-4, Phenylmagnesium chloride
RL: PRT (Reactant)
(**stereoselective** Grignard reaction of, with chiralamid derived from ephecrine and dichlorocinnamoyl chloride)

IT 100-[illegible]-3, Phenylmagnesium bromide
RL: PRT (Reactant)
(**stereoselective** reaction of, with chiralamid derived from ephedrine and dichlorocinnamoyl chloride)

IT 75-36-5, Acetyl chloride
RL: PRT (Reactant)
(use of, as esterification reagent in isomeric synthesis of (dichlorophenyl)dihydronaphthalenone)

IT 1310-[illegible]-3, Potassium hydroxide, uses
RL: USES (Uses)
(use of, as hydrolysis reagent in asym. synthesis of (dichlorophenyl)dihydronaphthalenone)

IT 7719-09-7, Thionyl chloride
RL: PRT (Reactant)
(use of, as reagent in asym. synthesis of (dichlorophenyl)dihydronaphthalenone)

IT 75-05-8, Acetonitrile, uses 108-88-3, Toluene, uses
RL: USES (Uses)
(use of, as solvent in isomeric synthesis of (dichlorophenyl)dihydronaphthalenone)

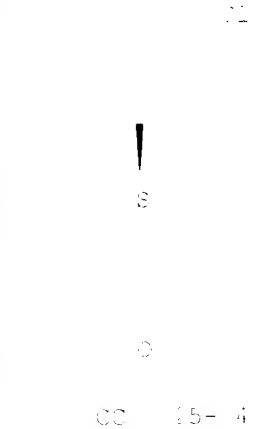
IT 60-29-7, Diethyl ether, uses 75-09-2, Methylene chloride, uses 107-21-1, 1,2-Ethanediol, uses 109-99-9, uses
RL: USES (Uses)
(use of, as solvent in isomeric synthesis of

(dichlorophenyl)dihydronaphthelnone)

=> d ibib abs hitstr IND 6

L31 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:212615 HCAPLUS
DOCUMENT NUMBER: 116:212615
TITLE: Synthesis of 4(S)- 3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone by SN2 cuprate displacement of an activated chiral benzylic alcohol
AUTHOR(S): Quallich, George J.; Woodall, Teresa M.
CORPORATE SOURCE: Process Res. Dev. Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Tetrahedron (1992), 48(47), 10239-48
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:212615
AB Two routes for the prepn. of the title compd. are reported. The more efficient route generates a chiral benzylic alc. by catalytic asym. oxazaborolidine redn. of a .gamma.-keto ester that is subsequently activated and displaced in an SN2 manner with a higher-order cuprate. Intramol. Friedel-Crafts cyclization of the resulting tert-Bu ester also affords the title compd.
IT **124379-29-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 15- 4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
ST chlorophenyldihydronaphthalenone; naphthalenone dichlorophenyldihydro
IT 112[illegible]-81-8
RL: RCT (Reactant)
(borane redn. of oxobutanoate in presence of)
IT 115-11-7, reactions
RL: RCT (Reactant)
(esterification of keto acid by)
IT 147[illegible]-16-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

IT 147189-[illegible]-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and desilylation of

IT 147[illegible]-42-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and intramol. cyclocondensation reaction of, naphthalenone
derivs. by)

IT 147[illegible]-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and methylation of)

IT 147[illegible]-48-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of)

IT 147[illegible]-51-2P 147213-46-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and phenylation of, copper salt-mediated)

IT 147[illegible]-00-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and phenylation of, copper-salt mediated)

IT 147[illegible]-03-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT 147[illegible]-09-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of, **stereoselective**)

IT 147189-91-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resoln. of)

IT 147[illegible]-94-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and silylation of)

IT **124379-29-9P** 147189-92-2P 147189-96-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT [illegible]-14-[illegible]
RL: RCT (Reactant)
(prepn. or esterification of, with tert-butanol)

IT [illegible]-43-[illegible]
RL: RCT (Reactant)
(resoln. by, of hydroxy acid)

=> d ibib abs hitstr 1-35

L32 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:660245 HCAPLUS
DOCUMENT NUMBER: 135:34019
TITLE: Novel process for preparing (+)-cis-sertraline
INVENTOR(S): Mandelovich, Mariaara; Nisam, Tammy; Pilarsky, Gideon; Gershon, Neomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068566	A1	20010920	WO 2001-US8090	20010314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189355 P 20000314
OTHER SOURCE(S): CASREACT 135:34019
AB (+)-Cis-sertraline hydrochloride was prepd. The present invention also includes processes for making sertraline having a cis/trans ratio greater than 5:1, greater than or equal to 8:1, or between about 8:1 and about 12:1, from the Schiff base of sertralone, sertraline-1-imine. E.g., hydrogenation of sertraline-1-imine in presence of Pd/C gave the cis/trans-sertraline (cis/trans = 95:1 to 12:1). Reacting cis/trans-sertraline with D-mandelic acid, followed by treatment with NaOH gave (+)-sertraline base, which was converted to (+)-sertraline hydrochloride.
IT **79560-19-3**
RL: RCT (Reactant)
(prepn. of (+)-cis-sertraline)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Cl

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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:380647 HCAPLUS
DOCUMENT NUMBER: 135:5456
TITLE: Preparation of dichlorophenyltetralonelmine isomer
INVENTOR(S): Thommen, Marc; Hafner, Andreas; Kelly, Roman; Kirner, Hans-Joerg; Brunner, Frederic
PATENT ASSIGNEE(S): Ciba Specialty Chemicals Holding Inc., Switz.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036377	A1	20010525	WO 2000-EP10970	20001107

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 1999-811055 A 19991116
OTHER SOURCE(S): MARPAT 135:5456
GI

X

R I

AB The title process comprises prepn. of title compd. I (R = C6H3Cl2-3,4, X = NMe) (II) from a mixt. comprised of I (X = O) III; R = C6H3Cl2-3,4) and III (R = C6H3Cl2-3,3) in which the mixt. is treated with MeNH2 in the presence of MeSO3H followed by, e.g., cooling of the reaction mixt. which produces an 88% yield of imine comprising 96.9% II.

IT **79560-19-3**
RL: FCT (Reactant)
prepn. of dichlorophenyltetralonemimine isomer)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:319858 HCAPLUS
DOCUMENT NUMBER: 134:326286
TITLE: Improved synthesis of racemic sertraline
INVENTOR(S): Fischer, Erik; Treppendahl, Svend Peter; Pedersen, Soren Bols
PATENT ASSIGNEE(S): A/S Gea Farmaceutisk Fabrik, Den.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030746	A1	20010503	WO 2000-DK546	20001010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DK 9901540	A	20010423	DK 1999-1540	19991027

PRIORITY APPLN. INFO.: DK 1999-1540 A 19991027
OTHER SOURCE(S): CASREACT 134:326286; MARPAT 134:326286

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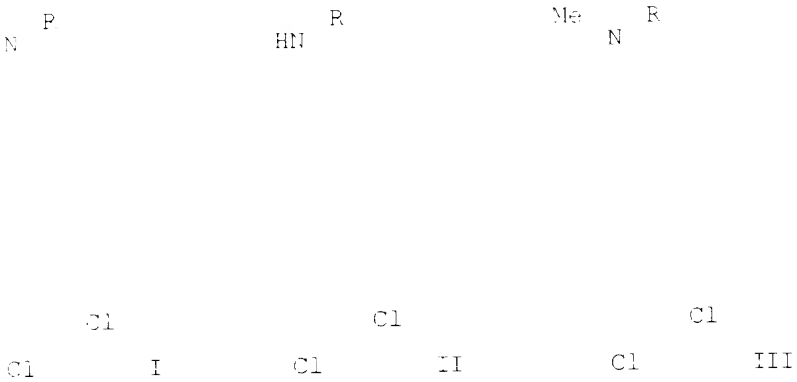

AB An process for the high-yield synthesis of sertraline, cis-(1S,(4S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine, is presented in which an imine [I; R = (un)substituted benzyl], prepd. by the imination of an amine RNH2 with the corresponding cyclic ketone, is hydrogenated to form a secondary amine (II) and then N-methylated or reductively N-methylated to form the corresponding tertiary methylamine (III) which is converted to sertraline or its salts by removal of the R group (e.g., hydrogenolysis). R-group-cleavable tertiary methylamine derivs. are prepd.

IT **79560-19-3**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
BL: RCT (Reactant)
(in an improved synthesis of racemic sertraline)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:167954 HCAPLUS
DOCUMENT NUMBER: 134:207602
TITLE: A reductive amination process for the preparation of

TI cis-(1S,4S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine hydrochloride from 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone and methylamine and hydrogen

AU INVENTOR(S): Vyas, Sharad Kumar
PA PATENT ASSIGNEE(S): India

SO SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT DOCUMENT TYPE: Patent
LA LANGUAGE: English
FAN.CNT FAMILY ACC. NUM. COUNT: 1
PI PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016089	A1	20010308	WO 2000-IB1185	20000828

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CA 1999-2279748 A 19990901
OTHER SOURCE(S): CASREACT 134:107602

AB There is disclosed a process for the prepn. of cis-(1S,4S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamin hydrochloride (i.e., sertraline hydrochloride) and the intermediate cis-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine hydrochloride, which comprises the reductive amination of 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone with methylamine and hydrogen in the presence of a catalyst such as Raney Nickel to produce the intermediate amine, treating that amine with hydrogen chloride to produce the corresponding cis- and trans-amine hydrochloride salts, isolating and purifying the amine hydrochloride mixt. to obtain the intermediate cis-amine hydrochloride, and converting the cis-amine hydrochloride into cis-(1S,4S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamin hydrochloride.

IT **79560-19-3**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone
RL: RCT (Reactant)
(reductive amination process for the prepn. of cis-(1S,4S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthaleneamine hydrochloride from 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone and methylamine and hydrogen using)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Cl

Cl

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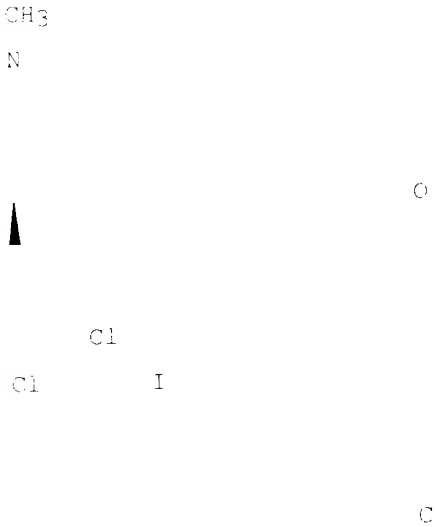
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

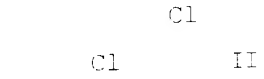
L32 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:376764 HCAPLUS
DOCUMENT NUMBER: 134:41980
TITLE: Process for preparing the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine from the (+) enantiomer of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenonetetralone
INVENTOR(S): Quallich, George Joseph
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1059287	A1	20001213	EP 2000-304724	20000605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000351758	A2	20001219	JP 2000-167473	20000605
CN 1277188	A	20001220	CN 2000-118079	20000608
BR 2000002606	A	20010102	BR 2000-2606	20000609

PRIORITY APPLN. INFO.: US 1999-138340 P 19990609
OTHER SOURCE(S): CASREACT 134:41980
GI



I



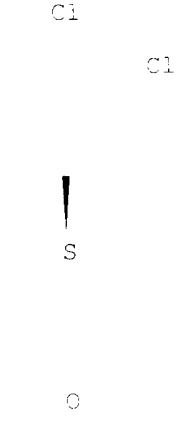
II

AB This invention relates to a novel improved process for prepg. the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine (I), an intermediate in the manuf. of sertraline, by reacting the (+) enantiomer of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (II) with monomethylamine and titanium chloride or mol. sieves. Subsequent I hydrogenation and salification-resoln. leads to the prepn. of a sertraline III salt.

IT **124379-29-9 155748-61-1**
RL: RCT (Reactant)
(process for prepg. the (+) enantiomer of N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine from the (+) enantiomer of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenonetetralone)

RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 155748-61-1 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).

Cl

Cl

B

O

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:772514 HCAPLUS
DOCUMENT NUMBER: 133:334855
TITLE: Transition metal dinuclear complexes with chiral carboxylate ligands as catalysts and methods for their preparation and use
INVENTOR(S): Davies, Huw M. L.
PATENT ASSIGNEE(S): The Research Foundation of State University of New York, USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064583	A1	20001102	WO 2000-US11287	20000426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173278	A1	20020213	EP 2000-926452	20000426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-129262 P 19990413
US 2000-521375 A 20000308
WO 2000-US11287 W 20000426

OTHER SOURCE(S): CASREACT 133:334855; MARPAT 133:334855
AB Transition metal dinuclear (in particular Ru and Rh) complexes with

chiral carboxylate ligands were prepd. as catalysts for carrying out C-H insertion reactions. Procedures for prepg. d-threo methylphenidate, tolterodine, CDP-840, nomifensine, and sertraline, are described. For example, Rh2L2 (H2L = 1,3-bis(S-2-N-2,4,6-triisopropylphenylsulfonyl)prolin-2-yl)benzene) was prepd. by the reaction of 1,3-diiodobenzene with N-Boc-pyroglutamic Et ester, followed by hydrogenation, reaction with 2,4,6-triisopropylphenylsulfonyl chloride, deprotection and reaction with Rh acetate. For example, Rh2L14 (H2L1 = S-4-dodecylphenylsulfonylproline) was used as a catalyst for highly regio-, diastereo- and enantioselective C-H insertions of aryldiazoacetates into cyclic N-Boc-protected amines.

IT **124379-29-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(rhodium chiral carboxylate dinuclear complexes as insertion reaction catalysts for aryldiazoacetates into amines)

RN 124379-29-9 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

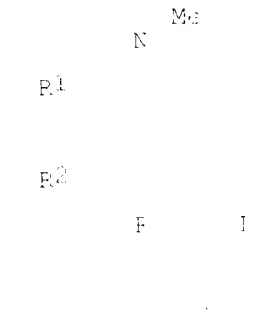
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:314668 HCAPLUS
DOCUMENT NUMBER: 132:321719
TITLE: Method of producing ketimines
INVENTOR(S): Trommer, Marc; Herold, Peter
PATENT ASSIGNEE(S): Ciba Specialty Chemicals Holding Inc., Switz.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026181	A1	20000511	WO 1999-EP7894	19991019

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1124784 A1 20010822 EP 1999-971411 19991019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: CH 1998-2201 A 19981030
WO 1999-EP7894 W 19991019
OTHER SOURCE(S): CASREACT 132:321715; MARPAT 132:321715
GI



AB Title compds. [I; R = (un)substituted Ph; R1R2 = (un)substituted CH:CHCH:CH] were prepd. by (1) reaction of the corresponding ketone with MeNH2 in a protic solvent and (2) the obtained I is purified by recrystn. and/or reaction step (a) is carried out in the presence of a catalyst.

IT **79560-19-3**
RL: RCT (Reactant)
(method of producing ketimines)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:250966 HCAPLUS
DOCUMENT NUMBER: 133:30359

TITLE: DDQ as a versatile reagent for oxidative cleavage of tosylhydrazones and oximes
AUTHOR(S): Chandrasekhar, S.; Reddy, Ch. Rami Reddy, M. Venkat
CORPORATE SOURCE: Indian Institute of Chemical Technology, Hyderabad, 500007, India
SOURCE: Chemistry Letters (2000), (4), 420-421
CODEN: CMLTAG; ISSN: 0366-7022
PUBLISHER: Chemical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was found to be a very efficient oxidative reagent for the selective cleavage of tosylhydrazones and oximes of carbonyl compds. for the first time. For example, treatment of benzaldehyde oxime with DDQ gave benzaldehyde in 90% yield. Similar treatment of 3-O-Methyl-1,2-O-(1-methylethylidene)pentodialdo-1,4-furanose [(4-methylphenyl)sulfonyl]hydrazone gave 3-O-methyl-1,2-O-(1-methylethylidene)pentodialdo-1,4-furanose in 85% yield.
IT **79560-19-3P**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of carbonyl compds. via oxidative cleavage of tosylhydrazones and oximes with DDQ)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:201560 HCAPLUS
DOCUMENT NUMBER: 132:238403
TITLE: Analysis of cis-trans isomers and enantiomers of sertraline by cyclodextrin-modified micellar electrokinetic chromatography
AUTHOR(S): Lucangioli, C. E.; Herrada, L. G.; Tripodi, V. P.; Rodriguez, V. G.; Lopez, E. F.; Rouge, P. D.; Carducci, C. N.
CORPORATE SOURCE: Faculty of Pharmacy and Biochemistry, Department of Analytical Chemistry and Physicochemistry, University of Buenos Aires, Junin, 956 (1113), Argent.
SOURCE: J. Chromatogr., A (2000), 871(1+2), 207-215
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this work development, optimization and validation of a cyclodextrin-modified micellar electrokinetic chromatog. (CD-modified MEKC) method is proposed to resolve sepn. of the sertraline hydrochloride and synthesis-related substances. Sertraline hydrochloride, the cis-(1S,4S) enantiomer form, is used as an antidepressant therapeutic agent. A buffer comon. composed of 20 mM sodium borate, pH 9.0 with 50 mM sodium cholate, 15 mM sulfated .beta.-cyclodextrin and 5 mM hydroxypropyl-.beta.-cyclodextrin was found to be the most suitable background electrolyte. Quantitation of the impurities at levels of 0.1% in different samples of the bulk drug was detd. A comparison of the results with those obtained by HPLC method01. was also accomplished. The method proved appropriate for testing the purity of sertraline hydrochloride in bulk drug.

IT **79560-19-3**

RL: ANT (Analyte); ANST (Analytical study)
(sepn. of enantiomeric forms of racemic cis-trans stereoisomers of sertraline and related substances by micellar electrokinetic chromatog.)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Cl

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REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2006 ACS

ACCESSION NUMBER: 2000:13482 HCAPLUS

DOCUMENT NUMBER: 132:334156

TITLE: Catalytic Asymmetric Synthesis of Diarylacetates and 4,4-Diarylbutanoates. A Formal Asymmetric Synthesis of (+)-Sertraline. (Erratum to document cited in CA131:1.87?6)

AUTHOR(S): Davies, Huw M. L.; Stafford, Douglas G.; Hansen, Tore

CORPORATE SOURCE: Dep. Chem., State Univ. New York at Buffalo, Buffalo, NY, 14260, USA

SOURCE: Org. Lett. (2000), 2(3), 417
CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society

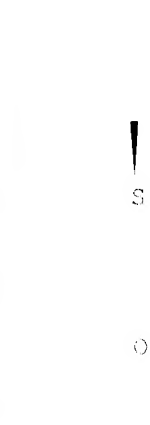
DOCUMENT TYPE: Journal

LANGUAGE: English

AB On page 733, the Rh2(S-DOSP)4-catalyzed C-H insertions of aryldiazoacetates 9 and 11 with 1,4-cyclohexadiene (Schemes 1 and 2) were carried out at =50.degree.C not at 23.degree.C as indicated in the paper. Detailed exptl. data are available in the Supporting Information.

IT **124379-29-9P**
RL: SPN (Synthetic preparation ; PREP (Preparation)
(catalytic asym. synthesis of diarylacetates, diarylbutanoates, and sertraline intermediate (Erratum))
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L32 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:713014 HCAPLUS
DOCUMENT NUMBER: 131:342429
TITLE: Preparation of 4-[(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-yliqene]methylamine from 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-one and methylamine in the absence of a dehydrating agent.
INVENTOR(S): Simig, Gyula; Kotay Nagy, Peter; Barkoczy, Jozsef; Krasznai, Gyorgy; Nagy, Kalman; Vereczkeyne Donath, Gyorgyi; Nemeth, Norbert; Szabo, Tibor; Sztruhar, Ilona; Ladanyi, Laszlo; Palans, Laszlo; Doman, Imre; Greff, Zoltan; Ratkai, Zoltan; Seres, Peter
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957095	A2	19991111	WO 1999-HU34	19990503
WO 9957095	A3	20000113		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9938401 A1 19991122 AU 1999-38401 19990503
PRIORITY APPLN. INFO.: HU 1998-10 4 19980505
WO 1999-HU34 19990503

OTHER SOURCE(S): CASREACT 131:336824
AB 4-[(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-ylidene]methylamine (I) was prepd. from 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-one (II) and MeNH2 in a lower alkanol in the absence of a dehydrating agent. Thus, MeNH2 in MeOH was added to II in MeOH at room temp. followed by 24 h, stirring to give 94.5% I.
IT **79560-19-3**
RL: RCT (Reactant)
(prepn. of 4-[(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-ylidene]methylamine from 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalene-1-one and methylamine in the absence of a dehydrating agent)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

C.

Cl

L32 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:723019 HCAPLUS
DOCUMENT NUMBER: 131:336824
TITLE: Process for the production of enantiomerically pure or optically enriched sertraline-tetralone using continuous chromatography
INVENTOR(S): Dapremont, Oliver; Geiser, Fiona; Zhang, Tong; Guhan, Subramanian S.; Guinn, Robert M.; Quallich, George J.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957089	A1	19991111	WO 1999-US9037	19990427
W: BR, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1073618	A1	20010207	EP 1999-920040	19990427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

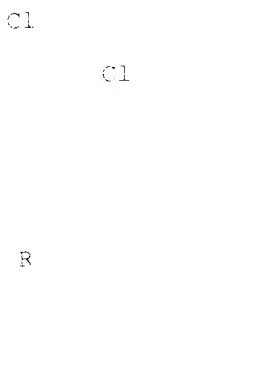
PRIORITY APPLN. INFO.: US 1998-83851 P 19980501
WO 1999-US9037 W 19990427

AB Enantiomerically pure or optically enriched sertraline-tetralone was obtained from a mixt. contg. two enantiomers using continuous chromatog. on a liq. mobile phase comprising at least one polar solvent and a solid chiral stationary phase comprising a derivatized polysaccharide that is selected from the amylosic, cellulosic, chitosan, xylan, curdlan, dextran, and inulan class of polysaccharides. Thus, racemic sertraline tetralone was chromatographed on a simulated moving bed of amylose 3-chloro-4-methylphenylcarbamate with MeCN as the mobile phase. The undesired (-)-isomer was eluted first and was racemized by treatment with NaOH in MeCN.

IT **155748-61-1**
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process)
(resoln. of sertraline-tetralone using continuous chromatog.)

RN 155748-61-1 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **79560-19-3P**
RL: PUR (Purification or recovery); PREP (Preparation)
(resoln. of sertraline-tetralone using continuous chromatog.)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

IT **124379-29-9P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(resoln. of sertraline-tetralone using continuous chromatog.)
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

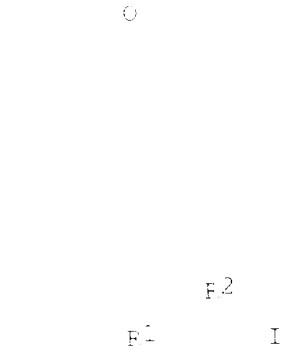
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:708727 HCAPLUS
DOCUMENT NUMBER: 131:323414
TITLE: Process for preparing 4-(substituted phenyl)-3,4-dihydro-2H-naphthalen-1-ones
INVENTOR(S): Odorisio, Paul Angelo; Pastor, Stephen Daniel; Shum, Sai Ping
PATENT ASSIGNEE(S): Ciba Specialty Chemicals Holding Inc., Switz.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955656	A1	19991104	WO 1999-EP2455	19990412
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6103948	A	20000815	US 1999-259720	19990301
AU 9935228	A1	19991116	AU 1999-35228	19990412

EP 1073617 A1 20010207 EP 1999-916913 19990412
R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE
PRIORITY APPLN. INFO.: US 1998-82812 P 19980423
WO 1999-EP2455 W 19990412

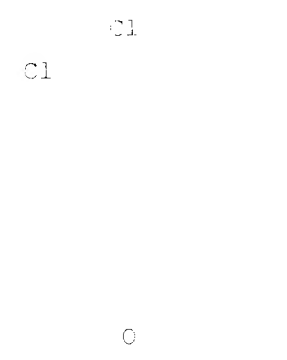
OTHER SOURCE(S): CASREACT 131:322419; MARPAT 131:322419
GI



AB 4-(Substituted phenyl)-3,4-dihydro-2H-naphthalen-1-ones (I; R1, R2 = H, Cl), useful as intermediates in the prepn. of antidepressant agents, are conveniently prepd. by reacting 1-COR3- or 1-Me3Si-substituted naphthalenes (R3 = C1-6 alkyl, Ph) with benzene derivs. 1,2-R1R2C6H4 (R1, R2 as above) in the presence of an acid catalyst. Thus, 4-(3,4-dichlorophenyl)-3,4-dihydro-2H-naphthalen-1-one, which is useful as an intermediate in the prepn. of the antidepressant sertraline, was prepd. by reacting 1-naphthyl acetate with 1,2-Cl2C6H4 in the presence of AlCl3 or AlBr3.

IT **79560-19-3P**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (dichlorophenyl)dihydronaphthalenone by phenylation of naphthyl acetate with dichlorobenzene)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:643943 HCAPLUS
DOCUMENT NUMBER: 131:243066
TITLE: Process for the preparation of racemic sertraline
INVENTOR(S): Briot, Patrick
PATENT ASSIGNEE(S): Cataly's, Fr.
SOURCE: Fr. Pat. Appl., 9 pp.
CODEN: FRXXIW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 947499	A2	19991006	EP 1999-400077	19990326
EP 947499	A3	20000223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2777900	A1	19991008	FR 1998-4270	19980401
US 6262308	B1	20010717	US 1999-280673	19990329

PRIORITY APPLN. INFO.: FR 1998-4270 A 19980401
OTHER SOURCE(S): CASREACT 131:243066
AB Racemic sertraline, cis-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthylamine, is prepd. in high yield and selectivity by the reaction of 4-(3,4-dichlorophenyl)tetralone with N-methylformamide in the presence of formic acid, followed by treatment of the reaction mixt. with a base (e.g., KOH), and a selective crystn. of the cis isomer is obtained by the addn. of an acid (e.g., aq. HCl).
IT **79560-19-3P**
RL: PCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(process for the prepn. of racemic sertraline)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:595119 HCAPLUS
DOCUMENT NUMBER: 131:214076
TITLE: Preparation of benzyl alcohol derivatives as intermediates for antidepressant sertraline
INVENTOR(S): Miyamoto, Hideto; Sugi, Kiyoshi; Itaya, Nobushige

PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946233	A1	19990916	WO 1999-JP1066	19990304

W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: JP 1998-51637 19980309
JP 1998-160463 19980609

OTHER SOURCE(S): CASREACT 131:214076; MARPAT 131:214076

AB Benzyl alc. derivs. 3,4-Cl2C6H3CH(OH)CH2CH2R1 (R1 = cyano, CO2R2; R2 = linear C1-5 alkyl), useful as intermediates for antidepressant sertraline, are prepd. by reaction of 3,4-dichlorobenzaldehyde with CH2:CHR1 and redn. of 3,4-Cl2C6H3COCH2CH2R1. Thus, reaction of 3,4-dichlorobenzaldehyde with acrylonitrile in the presence of NaCN gave 73.2% 4-(3,4-dichlorophenyl)-4-ketobutyronitrile, redn. of which with NaBH4 in MeOH in the presence of aq. NaOH gave 93.2% 4-(3,4-dichlorophenyl)-4-hydroxybutyronitrile.

IT **79560-19-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of benzyl alc. derivs. as intermediates for antidepressant sertraline)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:464264 HCAPLUS
DOCUMENT NUMBER: 131:116073
TITLE: Novel process for preparing a ketimine
INVENTOR(S): Dalberg, Juan Carlos; Pfisterer, David Michael; Taber, Geraldine Patricia
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

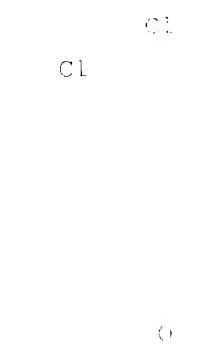
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9936394	A1	19990722	WO 1998-IB1619	19981015
W: AL, AM, AT, AU, AZ, BA, BB, BG, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9898746	A1	19990802	AU 1998-98746	19981015
BR 9814148	A	20001010	BR 1998-14148	19981015
EP 1043666	A1	20001011	EP 1998-949508	19981015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
US 6313360	B1	20011106	US 1999-380562	19990902
NO 2000003625	A	20000915	NO 2000-3625	20000714

PRIORITY APPLN. INFO.: US 1998-71600 P 19980116
WO 1998-IB1619 W 19981015

AB This invention relates to a novel improved process for prepn. of N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine I from 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone and monomethylamine. I is a pharm. intermediate in the prepn. of sertraline.

IT **79560-19-3**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: RCT (Reactant)
(prepn. of dichlorophenyldihydronaphthalenylidenemethanamine as a sertraline intermediate)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2004 ACS
ACCESSION NUMBER: 1999:34[illegible] HCAPLUS
DOCUMENT NUMBER: 131:129[illegible]
TITLE: Catalytic asymmetric synthesis of diarylacetates and 4,4-diarylbutanoates. A formal asymmetric synthesis of

(+)-sertraline

AUTHOR(S): Davies, Huw M. L.; Stafford, Douglas G.; Hansen, Tore
CORPORATE SOURCE: Department of Chemistry, State University of New York at Buffalo, Buffalo, NY, 14260, USA
SOURCE: Org. Lett. (1999), 1(2), 233-236
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:129734
GI

AB The intermol. C-H insertion chem. of phenyldiazoacetates, e.g., ArC(CO2Me):N2 (Ar = 4-ClC6H4, 4-MeC6H4, 4-MeOC6H4, 2-naphthyl), catalyzed by dirhodium tetrakis((S)-N-(dodecylbenzenesulfonyl)prolinate) (Rh2(S-DOSP)4) can be effectively carried out on cyclohexadienes, e.g., 1,4-cyclohexadiene, leading to the asym. synthesis of diarylacetates, e.g., 1. The reaction of vinyldiazoacetates, e.g., PhCH:CHC(CO2Me):N2, with cyclohexadienes results in an unprecedented carbenoid reaction that is formally a combined C-H insertion/Cope rearrangement. The synthetic utility of this novel transformation was demonstrated by its utilization in a formal asym. synthesis of (+)-sertraline.

IT **124379-29-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(catalytic asym. synthesis of diarylacetates, diarylbutanoates, and sertraline intermediate)

RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:423...
DOCUMENT NUMBER: 129:91571
TITLE: Novel intermediates for preparation of sertraline
INVENTOR(S): Vukics, Krisztina; Fodor, Tamas; Fischer, Janos; Fellegvari, Iren; Laszlo, Sandor
PATENT ASSIGNEE(S): Egyt Gyogyszervegyeszeti Gyar Rt., Hung.; Vukics, Krisztina; Fodor, Tamas; Fischer, Janos; Fellegvari, Iren; Laszlo, Sandor
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9827050	A1	19980625	WO 1997-HU83	19971215
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9854421	A1	19980715	AU 1998-54421	19971215
EP 946493	A1	19991006	EP 1997-951338	19971215
EP 946493	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, LV, FI, RO				
AT 229511	E	20021215	AT 1997-951338	19971215
US 6034274	A	20000307	US 1999-319379	19990727

PRIORITY APPLN. INFO.: HU 1996-3490 A 19961218
WO 1997-HU83 W 19971215

OTHER SOURCE(S): CASREACT 129:91571
AB Hydrogenation of the N-oxide of 1-methylamino-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalene (prepn. given) gives 61% cis-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-amine from which sertraline can be obtained by optical resoln.
IT **79560-19-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(novel intermediates for prepn. of sertraline
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

Cl

Cl

O

L32 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:239187 HCAPLUS
DOCUMENT NUMBER: 128:270446
TITLE: Improved process for the preparation of highly pure 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone, a pharmaceutical intermediate for the antidepressant sertraline
INVENTOR(S): Kotay, Nagy Peter; Barkoczy, Jozsef; Simig, Gyula; Sztunar, Ilona; Balazs, Laszlo; Doman, Imre; Greff, Zoltan; Ratkai, Zoltan; Seres, Peter; Clementis, Gyorgy; et al.
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.; Kotay Nagy, Peter; Barkoczy, Jozsef; Simig, Gyula; Sztuhar, Ilona; Balazs, Laszlo; Doman, Imre; Greff, Zoltan; Ratkai, Zoltan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815516	A1	19980416	WO 1997-HU58	19971008
W: AL, AM, AT, AU, AZ, BA, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BE, BF, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HU 218599	B	20000828	HU 1996-2762	19961009
AU 9748788	A1	19980505	AU 1997-48788	19971008
PRIORITY APPLN. INFO.:			HU 1996-2762 A	19961009
			HU 1997-1137 A	19970702
			WO 1997-HU58 W	19971008

OTHER SOURCE(S): CASREACT 128:270446
GI

AB The invention relates to a process for the prepn. of highly pure 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (I), an intermediate for the antidepressant sertraline. I is prepd. by reaction of o-dichlorobenzene and .alpha.-naphthol in a solvent medium in the presence of a Friedel-Crafts catalyst. The improvement comprises crystg. the crude reaction product at least once from a polar solvent and at least once from an apolar solvent, in either order, to reduce the amt. of the isomeric byproduct 4-(2,3-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (II) to below 1%. Redn. of the level of II to <1% eliminates the need for removal of corresponding isomeric contaminants at later stages, which is impractical. In 5 examples, using AlCl3 as the Friedel-Crafts reaction catalyst, MeOH as the polar crystn. solvent, and either n-hexane or MTBE as the apolar solvent, 58-68% yields of I were obtained. The purity of the crystd. I was 99.5%, with the content of II being below 0.5%.

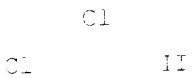
IT **79560-19-3P**, 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(improved prepn. of highly pure (dichlorophenyl)dihydronaphthalenone as an intermediate for sertraline)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:529824 HCAPLUS
DOCUMENT NUMBER: 127:247872
TITLE: General strategy toward the tetrahydronaphthalene

skeleton. An expedient total synthesis of sertraline

AUTHOR(S): Lautens, Mark; Kevis, Tomislav
CORPORATE SOURCE: Dep. Chem., Univ. Toronto, Toronto, ON, M5S 3H6, Can.
SOURCE: J. Org. Chem. (1997), 62(16), 5246-5247
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

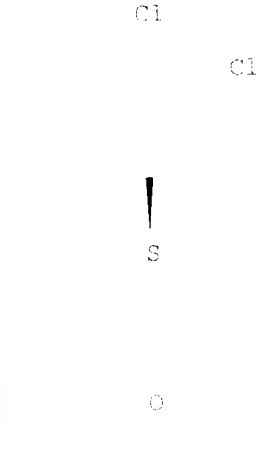


AB The ring opening of 1,4-epoxy-1,4-dihydronaphthalene with (S)-BINAP/Ni(COD)2 gave (R)-1,2-dihydro-1-naphthalenol (I). Protection of I followed by bromination, arylation with (3,4-dichlorophenyl)trimethylstannane, and sequential deprotection gave sertraline precursor II.

IT **124379-29-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(general strategy toward tetrahydronaphthalene skeleton and total synthesis of sertraline)

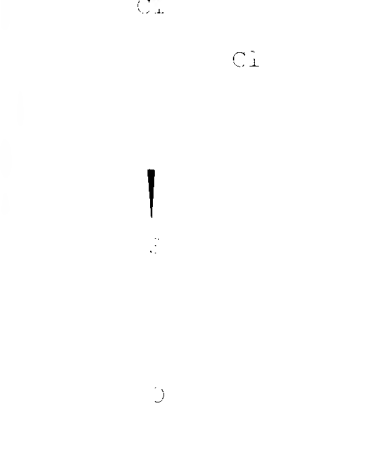
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L32 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:77337 HCAPLUS
DOCUMENT NUMBER: 126:196145
TITLE: Improved CEDIA benzodiazepine assay eliminates sertraline cross-reactivity
AUTHOR(S): Fitzgerald, Robert L.; Herold, David A.
CORPORATE SOURCE: Veterans Affairs Medical Center, Univ. California, San Diego, CA, 92161, USA
SOURCE: J. Anal. Toxicol. 1997, 21(1), 32-38
CODEN: JATODX; ISSN: 0146-4760
PUBLISHER: Preston Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Initial expts. demonstrated that the original CEDIA (cloned enzyme donor immunoassay) benzodiazepine assay cross-reacted with sertraline and sertraline metabolites. In response to this phenomenon, Boehringer Mannheim Corporation developed an improved CEDIA benzodiazepine assay in order to eliminate sertraline cross-reactivity. The improved CEDIA assay was evaluated against the original CEDIA product, EMIT II (enzyme multiplied immunoassay technique) benzodiazepine assay and electron capture neg. chem. ionization (ECNCI) gas chromatog.-mass spectrometry (GC-MS). Five hundred and thirty-one urine drug screens were tested by the immunoassays. Sensitivity and specificity of these immunoassays for the 5-aryl-7-chloro-1,4-benzodiazepine compds. were 92 and 98%, resp., for the improved CEDIA assay; 92 and 93%, resp., for the current CEDIA assay; and 87 and 98%, resp., for EMIT II. The improved CEDIA assay performed almost identically to the EMIT II assay, both of which had a significant advantage over the origin CEDIA product, which was subject to cross-reactivity because of sertraline metabolites. The .alpha.-hydroxyketone metabolites of sertraline are identified in human urine specimens for the first time using ECNCI GC-MS.
IT **124379-29-9**
RL: ANT (Analyte); ANST (Analytical study)
(improved CEDIA benzodiazepine assay for elimination of sertraline cross-reactivity in human urine)
RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L32 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:137914 HCAPLUS
DOCUMENT NUMBER: 124:317009
TITLE: Substituted (phenylureido)hexahydroazepinones and -tetrahydrobenzazepinones as selective CCK-B receptor antagonists useful in the treatment and prevention of gastrointestinal disorders, pain and anxiety disorders
INVENTOR(S): Lowe, John A., III
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 44 pp. Cont.-in-part of U.S. Ser. No. 825,677, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5494917	A	19960116	US 1993-78125	19930616
FI 7[illegible]	A2	19951030	FI 1994-2[illegible]	19[illegible]
CN 1074403	A	19930804	CN 1993-101155	19930121
ZA 9[illegible]	A	19940727	ZA 1993-5[illegible]	19930127
US 5[illegible]	A	19970701	US 1995-4[illegible]	19950607

PRIORITY APPLN. INFO.: US 1992-825677 19920127
US 1993-78125 19930616

OTHER SOURCE(S): MARPAT 124:317009
GI

AB The present invention relates to novel substituted hexahydroazepinones and tetrahydrobenzazepinones of the formulas I and II wherein Y1 and Y2 are independently selected from the group consisting of, e.g., Ph, thienyl, pyridyl, furyl, pyrimidyl; W1 and W2 are independently selected from, e.g., halo, nitro, amino; Z1 and Z2 are independently selected from the group consisting of, e.g., halo, (C1-C6) alkyl; R1 is Ph, CO2R2, SO2NR3R6 or CONR4R5, wherein said Ph may optionally be substituted with one or two substituents independently selected from halo, (C1-C6) alkyl, (C1-C6) alkoxy, nitro, amino and trifluoromethyl, and wherein R2, R3, R4, R5 and R6 are independently selected from hydrogen, (C5-C12) alkyl and fused, satd. carbocyclic systems contg. two or three rings, which are selective CCK-B receptor antagonists useful in the treatment and prevention of gastrointestinal disorders, pain and anxiety disorders (no data). Thus, e.g., bromination of 5-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one afforded diastereomeric 3-bromides; alkylation with N-tert-butyl-2-bromoacetamide to yield N-tert-butyl-2-[3-bromo-2-oxo-5-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepin-1-yl]ethanoic acid amide, azidation, hydrogenation (to the amine), and carbamoylation with m-tolyl isocyanate afforded N-tert-butyl-2-[3-(3-tolylureido)-2-oxo-5-phenyl-2,3,4,5-tetrahydro-1H-1-benzazepin-1-yl]ethanoic acid amide III.

IT **79560-19-3**
RL: RCT (Reactant)
(phenylureido)hexahydroazepinones and -tetrahydrobenzazepinones as selective CCK-B receptor antagonists)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:408900 HCAPLUS
DOCUMENT NUMBER: 121:8900
TITLE: Enantiomeric resolution of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone
INVENTOR(S): Lorenz, Douglas A.; Brose, Daniel J.
PATENT ASSIGNEE(S): Bend Research, Inc., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English.
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5348916	A	19940920	US 1993-36809	19930325
EP 617006	A2	19940928	EP 1994-301884	19940316
EP 617006	B1	19970730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 741703	A1	19970711	EP 1996-120170	19940316
EP 741703	B1	19990331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 166115	E	19980615	AT 1994-301884	19940316
ES 2118510	T3	19980916	ES 1994-301884	19940316
AT 179307	E	19990415	AT 1996-120170	19940316
ES 2132044	T3	19990801	ES 1996-120170	19940316
CA 2119674	AA	19940929	CA 1994-2119674	19940323
CA 2119674	C	19980414		
FI 9401376	A	19940926	FI 1994-1376	19940324
JP 07025718	A2	19950127	JP 1994-54438	19940324
PRIORITY APPLN. INFO.:			US 1993-36809	19930325
			EP 1994-301884	19940316

AB Enantiomers of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone (I) are resolved on an industrial scale by contacting racemic I with a homogeneous or nonhomogeneous liq. mixt. of a solvent (e.g., alcs. alkanes, ketones, etc.) and water, pure and unsupported .gamma.-cyclodextrin or its derivs. are added to form a selectively bound I enantiomer complex, the mixt. stirred or centrifuged to sep. the complex ppt., and the I enantiomer sepd. from the cyclodextrin complex by solvent extn.

IT **79836-44-5**
RL: PEOC (Process)

industrial-scale enantiomeric resoln. of, using .gamma.-cyclodextrins)

RN 79836-44-5 HCAPLUS
IT **124379-29-9P 155748-61-1P**
PL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by industrial-scale enantiomeric resoln. using .gamma.-cyclodextrins)
RN 124379-29-9 HCAPLUS
CN 1(2H -Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 155748-61-1 HCAPLUS
CN 1(2H -Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

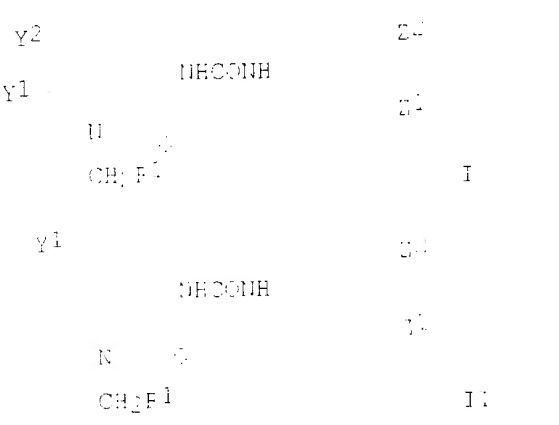
L32 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:191557 HCAPLUS
DOCUMENT NUMBER: 120:191557
TITLE: 3-(Phenylureido)azepin-2-ones and -benzazepin-2-ones useful as cholecystokinin receptor antagonists
INVENTOR(S): Lowe, John A., III
PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815539	A1	19980416	WO 1997-US18720	19971016
W: AU, BR, CA, IL, PL, RU, JP, KR, MX, NO, NZ, PH, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9848762	A1	19980501	AU 1998-48762	19971016
EP 931145	A1	19990728	EP 1998-950470	19971016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP [illegible]465	T2	20000704	JP 1998-[illegible]196	19971016
HU 7[illegible]4	A2	19991[illegible]	HU 1999-[illegible]195	19971016
BR 9712071	A	19991[illegible]	BR 1997-12071	19971016
CN 1274903	A	20001[illegible]	CN 1997-181158	19971016
ZA 9[illegible]5	A	19980[illegible]	ZA 1997-[illegible]	19971017
FI 9901513	A	19990706	FI 1999-1513	19990706
NO 9903[illegible]	A	19990[illegible]	NO 1999-[illegible]776	19990726

PRIORITY APPLN. INFO.: US 1996-28[illegible]07 19961017
WO 1997-US18720 19971016

OTHER SOURCE(S): MARPAT 128:191557
GI

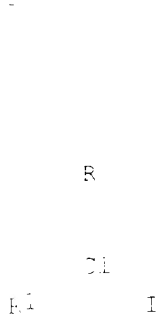


AB The title compds. I [R1 = unsubstituted Ph, CONR2, SO2NR3R4, CONR4R5; R2-R5 = H, C3-12 alkyl, fused and satd. carbocyclic systems contg. 2 or 3 rings; R6 = not defined; Y1, Y2 = (un)substituted Ph, (un substituted thienyl, (un)substituted pyridyl, (un substituted furyl, un substituted pyrimidyl, C3-8 (un)branched alkyl, C5-8 cycloalkyl; Z1, Z2 = halogen, C1-6 alkyl, C1-6 thioalkyl, C1-6 alkoxy, CF3, C1-6 carbalkoxy, NH2, NO2] and II, useful as cholecystokinin receptor antagonists [no data], are prepd. Thus, N-tert-Bu 2-[2-[3-(3-methylureido)-2-oxo-5-phenyl-2,3,4,5-tetrahydro-1H-(1)benzazepin-1-yl]ethanthio amide (m.p. 262-266.degree.) was prepd. from 5-phenyl-2,3,4,5-tetrahydro-1H-(1)benzazepin-2-one in 5 steps.

IT **79560-19-3**

RL: RCT (Reactant)
(reaction of, in prepn. of cholecystokinin receptor antagonist)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:106497 HCAPLUS
DOCUMENT NUMBER: 120:106497
TITLE: Condensation of 1-naphthol with ortho-dichlorobenzene in the presence of aluminum halides
AUTHOR(S): Repinskaya, I. B.; Koltunov, K. Y.
CORPORATE SOURCE: Novosib. Gos. Univ., Novosibirsk, Russia
SOURCE: Sib. Khim. Zh. (1993), (3), 73-6
CODEN: SKZHEC
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 120:106497
GI



AB The title reaction in the presence of AlBr3 or AlCl3 gave tetralones I (R = H, R1 = Cl; R = Cl, R1 = H), the product ratio depending on the reaction conditions.
IT **79560-19-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX

NAME)

Cl

Cl

)

L32 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:670823 HCAPLUS
DOCUMENT NUMBER: 119:270823
TITLE: Preparation of (4S)-4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone as a sertraline intermediate
INVENTOR(S): Quallich, George J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317662	A1	19930624	WO 1992-US7654	19920915
W: AU, CA, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9[illegible]	A1	19930714	AU 1992-25[illegible]	19920915
AU 6[illegible]	B2	19960822		
EP 6[illegible]	A1	19941117	EP 1992-92[illegible]	19920915
EP 6[illegible]	B1	19961113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP [illegible]02504	T2	19950316	JP 1992-[illegible]	19920915
HU 67623	A2	19950428	HU 1994-[illegible]	19920915
HU [illegible]	B	20010[illegible]		
AT [illegible]	E	19961115	AT 1992-[illegible]	19920915
ES [illegible]	T3	19970116	ES 1992-[illegible]	19920915
CA [illegible]	C	19970826	CA 1992-[illegible]	19920915
IL [illegible]	A1	19980622	IL 1992-[illegible]	19921107
ZA [illegible]	A	19940621	ZA 1992-[illegible]	19921111
US [illegible]	A	19941114	US 1993-[illegible]	19930609
FI [illegible]	A	19940610	FI 1994-[illegible]	19940610
NO [illegible]	A	19940613	NO 1994-[illegible]	19940610

PRIORITY APPLN. INFO.: US 1991-765019 A1 19911213
WO 1992-US7654 A 19920915

AB 3,4-Cl2C6H3COCH2CH2CO2H was esterified with Me2SO4:CH2 and the product reduced by BH3 in the presence of (S)-tetrahydro-1-methyl-3,3-diphenyl-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaborole to give, after mesylation, (R)-3,4-Cl2C6H3CHRCH2CR2CO2CMe3 (I; R = CH2OMe) which was treated with (Ph2Cu(CN)Li2) to give I (R = Ph). The latter was heated [illegible] h at

70. degree. with CF3SO2H in benzene to give the title compd. of 86% optical purity.

IT **124379-29-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as sertraline intermediate)

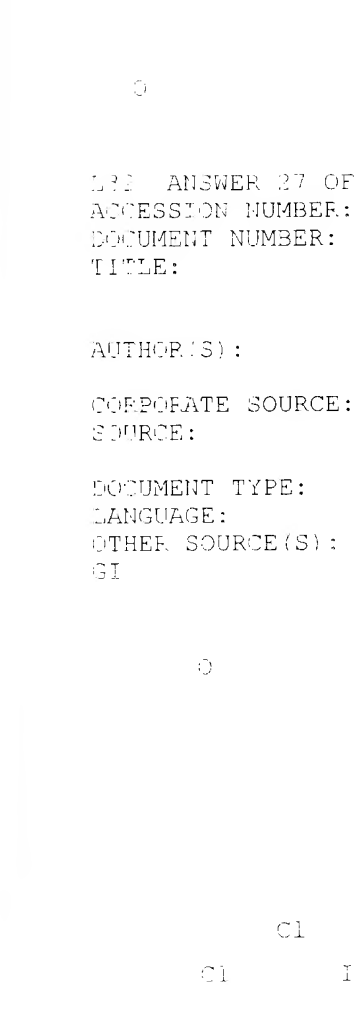
RN 124379-29-9 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L91 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:497154 HCAPLUS
DOCUMENT NUMBER: 113:97154
TITLE: Friedel-Crafts synthesis of 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenone, a key intermediate in the preparation of the antidepressant sertraline
AUTHOR(S): Quallich, George J.; Williams, Michael T.; Friedmann, Robert C.
CORPORATE SOURCE: Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA
SOURCE: J. Org. Chem. (1990), 55(16), 4971-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:97154
GI



AB An improved synthesis of the title compd. (I) from succinic annydride and 1,2-C12C6H4, which employs 3 Friedel-Crafts reactions to construct all of the C-C bonds and a chemoselective ketone redn., is reported.

IT **79560-19-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate in synthesis of sertraline)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

C.

Cl

L32 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:235002 HCAPLUS
DOCUMENT NUMBER: 112:235002
TITLE: Preparation of 4-(disubstituted aryl)-1-tetralones as intermediates for serotonin antagonists
INVENTOR(S): Adrian, Guy
PATENT ASSIGNEE(S): Delalande S. A., Fr.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 346234	A1	1989[illegible]	EP 1989-401577	19890607
EP 346234	B1	1993[illegible]		
R: AT, BE, CH, DE, ES, GB, GR, IT, LI, LU, NL, SE				
FR 2632623	A1	19891215	FR 1988-7641	19880608
FR 2632623	B1	1990[illegible]		
DK 8902[illegible]	A	1989[illegible]	DK 1989-2781	19890607
DK 171202	B1	1996[illegible]		
AT 84741	E	1993[illegible]	AT 1989-401577	19890607
ES 2044844	T3	1994[illegible]	ES 1989-401577	19890607
JP 02036142	A2	1990[illegible]	JP 1989-146746	19890608
JP 2814855	B2	1998[illegible]		
US 5014[illegible]	A	1991[illegible]	US 1989-363251	19890608
PRIORITY APPLN. INFO.:			FR 1988-7641	19880608
			EP 1989-401577	19890607

OTHER SOURCE(S): MARPAT 112:235002
GI For diagram(s), see printed CA Issue.
AB The title compds. (I; X = halo, alkyl, alkoxy; Y = 2'- or 3'-halo or

-alkyl) were prepd. by condensation reaction of .alpha.-naphthol (II) with disubstituted benzenes in the presence of an acid. Thus, II was stirred 5 h at 65.degree. with 3-ClC6H4C. and AlCl3 to give 61% I (X = Cl, Y = 3'-Cl).

IT **79560-19-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for serotonin antagonists)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

C.

Cl

L32 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:98231 HCAPLUS
DOCUMENT NUMBER: 112:98231
TITLE: Process for preparing a ketimine, N-[4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine
INVENTOR(S): Spavins, James C.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4855500	A	19890808	US 1988-190300	19880504
EP 341015	A2	19891108	EP 1989-304385	19890502
EP 341015	A3	19900124		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 02015053	A2	19900118	JP 1989-113561	19890502
CA 1329499	A1	19940719	CA 1989-598472	19890502
DK 8902180	A	19891105	DK 1989-2180	19890503
FI 8902139	A	19891105	FI 1989-2139	19890503
PRIORITY APPLN. INFO.:			US 1988-190300	19880504

OTHER SOURCE(S): CASREACT 112:98231

AB The title compd. (I) an intermediate for the known antidepressant sertraline is prepd. by a 1-step process by condensing 4-(3,4-dichlorophenyl)-3,4-dichydro-1 (2H)-naphthalenone (II) with MeNH2 in presence of a hydratable mol. sieve having a pore that is .gtoreq.3.ANG. as catalyst, whereby H2O is removed from the resulting reaction. The reaction takes place at 20-100.degree. and at pressure 1-10 atm. I, MeNH2

and powd. mol. sieve (activated) type No. 5 (Linde) were reacted for 4 h to give 37% I.

IT **79560-19-3**
RL: RCT (Reactant)
(condensation of, with methylamine, mol. sieve catalyst for)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

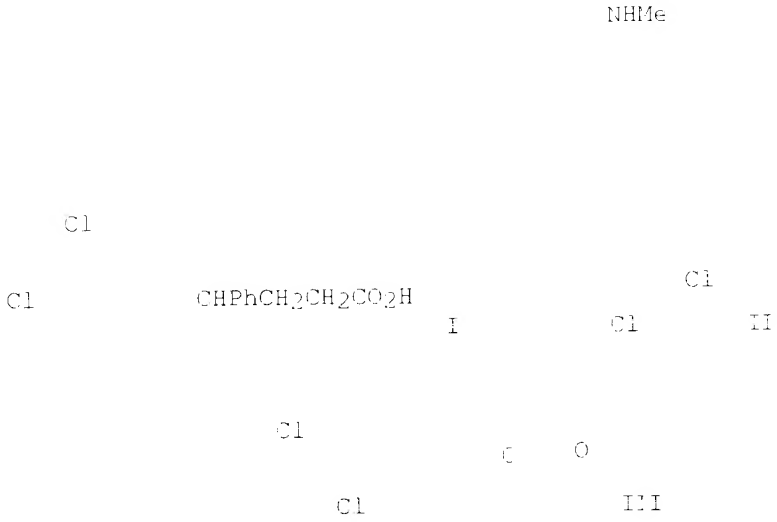
C1

C1

L32 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:55524 HCAPLUS
DOCUMENT NUMBER: 112:55242
TITLE: Preparation 4-(3,4-dichlorophenyl)-4-phenylbutanoic acid as an intermediate for the antidepressant sertraline
INVENTOR(S): Quallich, George J.; Williams, Michael T.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 9 pp. Cont.-in-part of U.S. 4,777,288.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4839104	A	19890613	US 1988-207579	19380616
US 4777288	A	19881011	US 1987-60577	19370611
PRIORITY APPLN. INFO.:			US 1987-60577	19370611

GI



AB The title acid I, useful as an intermediate for the antidepressant sertraline (II), is prepd. by an improved 3-step process. Heating 3,4-Cl2C6H3COCH2CH2CO2H with aq. NaOH at 70-80.degree. and then with NaBH4/NaOH at 65.degree. gave 3,4-Cl2C6H3CH(OH)CH2CH2CO2H which was heated with 5.3 N HCl at 57-60.degree. to give 92% furanone deriv. III. III was added to a slurry of AlCl3 and C6H6 in CH2Cl2 and the mixt. stirred 2 h at room temp. to give 91% I.

IT **79560-19-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of sertraline)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:15383 HCAPLUS
DOCUMENT NUMBER: 112:15383
TITLE: Metabolism and disposition of the 5-hydroxytryptamine uptake blocker sertraline in the rat and dog
AUTHOR(S): Tremaine, Larry M.; Welch, Willard M.; Ronfeld, Robert A.

CORPORATE SOURCE: Drug Metab. Dep., Pfizer, Inc., Groton, CT, USA
SOURCE: Drug Metab. Dispos. (1989), 17(5), 542-50
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

AB Sertraline (I) is a potent and selective inhibitor of neuronal serotonin uptake and is currently under development for the treatment of depression and of obesity. The drug was >97% bound to plasma proteins, yet extensively distributed into tissues. The whole brain concn. of sertraline in the rat was >40-fold higher than that in plasma, and the vol. of distribution was about 25 L/kg in the rat and dog. Sertraline was extensively metabolized by the rat and dog prior to excretion.. The metabolic clearance of sertraline was >35 mL of blood/min/kg in each species, and 1st-pass metab. occurred with oral administration. Initial metabolic steps included N-demethylation, N-hydroxylation, oxidative deamination, and glucuronidation of sertraline carbamic acid, which in rabbit was an equal. with sertraline and CO2. The N-demethyl metabolite, which was 10-fold less potent as an inhibitor of serotonin uptake, was formed in both species. Plasma area under the concn.-time curve for demethylsertraline was 66-170% of that for sertraline, and was dependent on the species examd. and route of drug administration. Sertraline and demethylsertraline underwent oxidative deamination to the corresponding ketone, which was subsequently hydroxylated at the .alpha.-carbon, forming a diastereomeric metabolite pair. The glucuronides of sertraline carbamic acid, N-hydroxysertraline, and the .alpha.-hydroxy ketone diastereomers comprised 15% and 82% of the total radiolabel excreted in urine plus bile of duct-cannulated rats and dogs, resp. Bile was the major route of elimination in both species.

IT **124379-29-9**
RL: FORM (Formation, nonpreparative)
(formation of, as sertraline metabolite

RN 124379-29-9 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT **79836-44-5**
FL: RCT (Reactant)
(reaction of, with monomethylamine)
RN 79836-44-5 HCAPLUS

L22 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:413113 HCAPLUS
DOCUMENT NUMBER: 105:13113
TITLE: Antidepressant derivatives of trans-4-phenyl-1,2,3,4-tetrahydro-1-naphthalenamine
INVENTOR(S): Welch, Willard M., Jr.; Harrert, Charles A.; Koe, B. Kenneth; Kraska, Allen R.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 90,237, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4[illegible]	A	1985[illegible]	US 1980-184447	19800905
EP [illegible]	A1	1981[illegible]	EP 1980-302810	19800818
EP [illegible]	B1	1983[illegible]		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT [illegible]	E	1983[illegible]	AT 1980-302810	19800818
JP [illegible]	A2	1981[illegible]	JP 1980-151995	19801029
JP [illegible]	B4	1986[illegible]		
FI [illegible]	A	1981[illegible]	FI 1980-3349	19801030
FI [illegible]	B	1986[illegible]		
FI [illegible]	C	1986[illegible]		
CA [illegible]	A1	1982[illegible]	CA 1980-363571	19801030
IL [illegible]	A1	1984[illegible]	IL 1980-61376	19801030
DK [illegible]	A	1981[illegible]	DK 1980-4624	19801031
DK [illegible]	B	1989[illegible]		
DK [illegible]	C	1990[illegible]		
NO [illegible]	A	1981[illegible]	NO 1980-3259	19801031
NO [illegible]	B	1986[illegible]		
NO [illegible]	C	1987[illegible]		
AU [illegible]	A1	1981[illegible]	AU 1980-63898	19801031

AU 517842	B2	19810827			
ES 496441	A1	19810116	ES 1980-496441	19801021	
ES 506893	A1	19820901	ES 1981-506893	19811105	
JP 58-222017	A2	19831223	JP 1983-78878	19830504	
JP 61-10046	B4	19860326			

PRIORITY APPLN. INFO.: US 1979-90237 19791101
US 1980-184447 19800905
EP 1980-303810 19801028

OTHER SOURCE(S): CASREACT 105:12113

GI

NR-R2

W

I

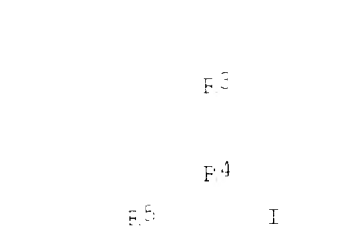
AB Trans-isomeric derivs. of 4-phenyl-1,2,3,4-tetrahydro-1-naphthalenamine, I where R1 = H or C1-3 normal alkyl, R2 = C1-3 normal alkyl, Z = C6H3(X)Y, X and Y = H, F, Cl, Br, CF3, C1-3 alkoxy, and CN (stereoreq.l of X and Y not H), and W = H, F, Cl, Br, CF3, and C1-3 alkoxy, are antidepressants. The preferred compd. is trans-(1S)(1R)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenamine (II). The synthesis, formulation, and biol. activity of the compds. is described. E.g., 3,4-dichlorobenzoyl chloride was reacted with benzene and the resultant 3-ethoxycarbonyl-4-(3,4-dichlorophenyl)-4-phenylbut-3-enoic acid hydrolyzed and decarboxylated. The product, 4-(3,4-dichlorophenyl)-4-phenylbut-3-enoic acid was reduced to 4-(3,4-dichlorophenyl)-4-phenylbutanoic acid which was cyclized to 4-(3,4-dichlorophenyl)-3,4-dihydro-1-(2H)-naphthalenone. The latter was converted to the Schiff base with Me3N and reduced to trans-(1S)(1R)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenamine-HCl. Resoln. afforded II-HCl and the corresponding 1S enantiomer. Tablets were prepd. from II-HCl 50, Na citrate 25, alginic acid 15, PVP 10, and Mg stearate 5 parts by wt. II-HCl reduced behavioral despair in mice as detd. by the Modified Persolt Method.

IT **79560-19-3P**
RL: RCT (Reactant); PREP (Preparation)
(prepn. and conversion to Schiff base and redn. of)

RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:622093 HCAPLUS
DOCUMENT NUMBER: 101:222093
TITLE: Nortricyclic antidepressant agents derived from cis- and trans-1-amino-4-aryltetralins
AUTHOR(S): Welch, Willard M.; Kraska, Allen R.; Sarges, Reinhard; Koe, B. Kenneth
CORPORATE SOURCE: Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA
SOURCE: J. Med. Chem. (1984), 27(11), 1508-15
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 101:222093
GI



AB The title compd. enantiomers I (R1 and R2 = H or Me; R3 = H, Cl, or MeO; R4 = H, Cl, CF3, or MeO; R5 = H, Br, Cl, F, CF3, MeO, BuO, or PhO) mostly as the HCl salts were prepd. from the appropriate benzophenone and 136 1-tetralone [52758-06-2] and evaluated in vitro for their ability to inhibit the uptake of dopamine and serotonin in corpus striatum and of epinephrine in hypothalamus of rats. The cis compds. are potent and selective inhibitors of serotonin uptake, whereas the trans compds. block uptake of dopamine and norepinephrine. Structure-activity relations are discussed.

IT **79560-19-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and imination-reaction of)

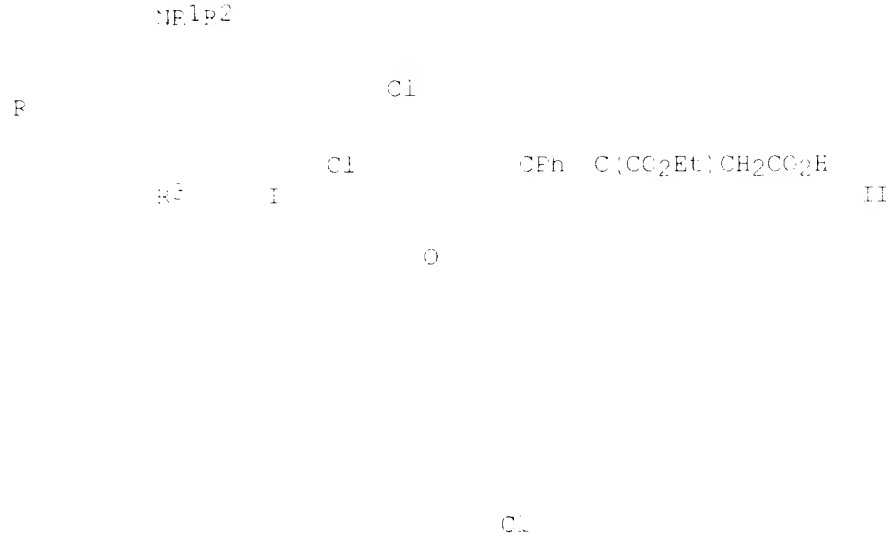
RN 79560-19-3 HCAPLUS

CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

L32 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:34934 HCAPLUS
DOCUMENT NUMBER: 96:34934
TITLE: Antidepressant derivatives of trans-4-phenyl-1,2,3,4-tetrahydro-1-naphthalenamine and pharmaceutical compositions
INVENTOR(S): Welch, Willard McKowan; Harbert, Charles Armon; Koe, Billie Kenneth; Kraska, Allen Richard
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 18401	A1	19810520	EP 1980-302810	19801028
EP 18401	B1	19830302		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4296676	A	19811203	US 1980-194447	19800905
AT 2667	E	19830315	AT 1980-303810	19801028
PRIORITY APPLN. INFO.:			US 1979-90237	19791101
			US 1980-194447	19800905
			EP 1980-303810	19801028

GI



AB Title compds. I (R = H, F, Cl, Br, F3C, alkoxy; R1 = H, alkyl; R2 = alkyl; R3 = optionally substituted Ph) were prepd. Thus, 3,4-Cl2C6H3COCl was alkylated using AlCl3 in benzene to give 3,4-Cl2C6H3COPh which was treated sequentially with Me3COK and (EtO2CCH2)2 to give II. II was decarboxylated and then hydrogenated to give 3,4-Cl2C6H3CHPhCH2CH2CO2H which was treated with SOCl2 and AlCl3 to give III. III was treated with MeNH2 to give trans-I (R = R2 = H, R1 = Me, R3 = 3,4-Cl2C6H3) (IV). IV blocked synaptosomal uptake of serotonin, dopamine, and norepinephrine by 50% at 1.05 .mu.mole/L, 0.05 .mu.m/L, and 0.12 .mu.m/L, resp., in rats.

IT **79836-44-5P**
RL: PCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
prepn. and alkyl amination of)

RN 79836-44-5 HCAPLUS

L32 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:609649 HCAPLUS
DOCUMENT NUMBER: 95:209649
TITLE: Antidepressant derivatives of cis-4-phenyl-1,2,3,4-tetrahydro-1-naphthalenamine and pharmaceutical compositions thereof
INVENTOR(S): Welch, Willard McKowan; Harbert, Charles Armon; Koe, Billie Kenneth; Kraska, Allen Richard
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 54 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 30081	A1	19810610	EP 1980-303809	19801028
EP 30081	B1	19830302		

R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

US 4[illegible]518	A	19[illegible]70	US 1979-90240	19791101
DK 8[illegible]52	A	19[illegible]02	DK 19[illegible]2	19[illegible]19
DE 19[illegible]52	B	19[illegible]11		
DE 19[illegible]3	C	19[illegible]19		
IN 1[illegible]43	A	19[illegible]81	IN 19[illegible]39	19[illegible]27
HU 2[illegible]	C	19[illegible]19	HU 19[illegible]	19[illegible]24
HU 1[illegible]4	B	19[illegible]20		
AT 2[illegible]	E	19[illegible]11	AT 19[illegible]809	19[illegible]24
SU [illegible]4467	A3	19[illegible]27	SU 19[illegible]8197	19[illegible]24
CS 2[illegible]9	B2	19[illegible]20	CS 19[illegible]14	19[illegible]24
FI [illegible]69	A	19[illegible]81	FI 19[illegible]	19[illegible]30
FI 6[illegible]	B	19[illegible]71		
FI 6[illegible]	C	19[illegible]11		
DD [illegible]19	C	19[illegible]13	DE 19[illegible]24740	19[illegible]30
CA [illegible]28	A1	19[illegible]31	CA 19[illegible]68	19[illegible]30
DD [illegible]5	A5	19[illegible]12	JP 19[illegible]128	19[illegible]30
IL [illegible]4	A1	19[illegible]11	IL 19[illegible]76	19[illegible]30
HU [illegible]58	A	19[illegible]81	IE 19[illegible]	19[illegible]31
NO 14[illegible]	B	19[illegible]13		
DK 14[illegible]	C	19[illegible]19		
AU [illegible]7	A1	19[illegible]	AT 19[illegible]	19[illegible]
AT [illegible]	B1	19[illegible]		
JP [illegible]137	A2	19[illegible]1	JP 19[illegible]698	19[illegible]1
JP [illegible]94	B4	19[illegible]12		
ZA [illegible]26	A	19[illegible]	ZA 19[illegible]6	19[illegible]1
ES [illegible]3	A1	19[illegible]10	ES 19[illegible]443	19[illegible]31
SU [illegible]2	A3	19[illegible]7	SU 19[illegible]5759	19[illegible]28
ES [illegible]	A1	19[illegible]1	ES 19[illegible]392	19[illegible]5
ES [illegible]	B2	19[illegible]16	SU 19[illegible]	19[illegible]1
CS [illegible]6	B2	19[illegible]16	SU 19[illegible]	19[illegible]1
IN 15[illegible]4	A	19[illegible]0	IN 19[illegible]	19[illegible]0
PRIORITY APPLN. INFO.:			US 1979-[illegible]	19[illegible]1
			IN 1980-[illegible]	19[illegible]7
			EP 1980-[illegible]	19[illegible]9
			CS 1980-[illegible]	19[illegible]9

GI

[illegible]

R4

[illegible] I

AB Antidepressant pharmaceuticals comprise the title compds. I [R1 = H or C1-4 alkyl; R2 = C1-3 alkyl; R3 = substituted Ph; R4 = H, Et, Cl, F, CF3, and C1-3 alkoxy) and their salts. I were prepd. by stepwise reaction either from the base-catalyzed Stobbe condensation of a substituted benzophenone with di-Et succinate or from the condensation of a tetralone with the appropriate secondary amine in the presence of an acid catalyst. Thus, a tablet formulation contained by wt. cis-(1S)-N-methyl-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthalenamine-HCl [79[illegible]-97-0] 50, Na citrate 25, alginic acid 10,

poly(vinylpyrrolidone) 10, and Mg stearate 5. The effectiveness of I in blocking synaptosomal uptake of serotonin was demonstrated.

IT **79560-19-3P**
RL: PREP (Preparation)
(prepn. and condensation with methylamine)

RN 79560-19-3 HCAPLUS
CN 1(2H)-Naphthalenone, 4-(3,4-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)